Bryan Hurlbutt (ISB # 8501)
Laurence ("Laird") J. Lucas (ISB # 4733)
Advocates for the West
P.O. Box 1612
Boise, ID 83701
208.342.7024
bhurlbutt@advocateswest.org
llucas@advocateswest.org

Attorneys for Nez Perce Tribe and Idaho Conservation League

Julia Thrower (ISB # 10251)
Mountain Top Law PLLC
614 Thompson Ave.
McCall, ID 83638
208.271.6503
jthrower@mtntoplaw.com

Attorney for Save the South Fork Salmon

BEFORE THE BOARD OF ENVIRONMENTAL QUALITY
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047	)	Agency Case No. 0101-22-01
	)	OAH Case No. 23-245-01
NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTH FORK SALMON	)	**EXPERT DECLARATION OF IAN H. VON LINDERN, P.E., Ph.D.**
Petitioners,	)	
v.	)	
IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY,	)	
Respondent,	)	
and	)	
PERPETUA RESOURCES IDAHO, INC.	)	
Intervenor-Respondent.	)	

I, Ian H. von Lindern, P.E., Ph.D., hereby declare under penalty of perjury and pursuant to the law of the State of Idaho that the foregoing is true and correct:

QUALIFICATIONS

Name and Affiliation

1. My name is Ian von Lindern. I reside in Moscow, Idaho. I am a licensed Professional Engineer in Chemical Engineering in Idaho (License # 3044). I have practiced in the disciplines of Environmental Engineering and Risk Assessment in Idaho for the last 50 years. I was President and Principal Scientist for TerraGraphics Environmental Engineering with offices in Moscow, Kellogg, and Boise, Idaho for 30 years, retiring in 2016. TerraGraphics was the Idaho Department of Environmental Quality's (DEQ) prime consultant for the Bunker Hill Superfund Site (BHSF) and I was Project Manager and lead risk assessor for both the BHSF and the Coeur d'Alene Basin Superfund Sites from 1984 to 2014.

2. Since retiring from the consulting business, I co-founded the non-profit humanitarian organization TerraGraphics International Foundation (TIFO) and have continued to work in mining-related health and safety issues in low-income countries. TIFO's mission is to assist mining and mineral processing communities to operate as safely as practicable while maintaining essential economic activities. In that regard, we support scientifically sound and transparent analyses of the environmental and human health issues faced by mining communities, and the development of local solutions implemented within community socio-economic and cultural capabilities. Under my direction in the last ten years, TIFO has conducted and completed site characterization, risk assessment, and risk mitigation projects in

Russia, China, Peru, Dominican Republic, Senegal, Nigeria, Kyrgyzstan, Uzbekistan, and the Duck Valley Shoshone Paiute Reservation in Idaho and Nevada.

Education and Experience

3. I hold a B.S. degree in Chemical Engineering from Carnegie-Mellon University, Pittsburgh, Pennsylvania and Masters and Ph.D. degrees in Environmental Science and Engineering from Yale University, New Haven Connecticut, specializing in air pollution and public health. I have served on numerous advisory committees and the U.S. Environmental Protection Agency's (EPA) Science Advisory Board and Clean Air Science Advisory Committee on several occasions from 1975 to 2018, advising on topics relating to exposure and risk assessment in childhood heavy metal poisoning. During that tenure, I directed more than 30 major environmental health investigations at mining and smelting sites, both nationally and internationally. A current C.V. is attached.[1]

Relevant Projects and Assignments

4. I was the Regional Environmental Engineer for DEQ's predecessor agencies in both the Coeur d'Alene and Twin Falls offices. In that capacity, I processed air quality permits for the Agency for several years at the major mining and smelting operations in the State during the 1970s, and early 1980s, including the Bunker Hill Mining and Metallurgical Complex, the last U.S. operational antimony smelter at Big Creek, Idaho, and numerous mining operations in North and Central Idaho. I designed and directed the implementation of the Silver Valley Lead Health Study that investigated and provided emergency response to the childhood lead poisoning epidemic in the Coeur d'Alene mining district in the 1970-80s.

[1] Exhibit A.

5. I have particular experience with implementing EPA risk assessment guidance in Idaho. Beginning in 1984, DEQ's predecessor, Idaho Department of Health and Welfare-Division of Environment (IDHW-DOE) was the lead agency implementing the Risk Assessment and Cleanup Management Plan developed for the populated areas of the Bunker Hill Superfund Site (BHSS). The BHSS was the U.S. second largest Superfund site, and IDHW-DOE was among the first health/environmental agencies to implement the EPA Risk Assessment Guidance for Superfund (RAGS) in the late 1980s.

6. As Project Manager, I was responsible for developing and implementing the risk assessment/risk management protocols, and cleanup plan for the BHSS in collaboration with several State, federal, tribal, local governments, and industry. The project was monitored and collaboratively developed by several entities including EPA Regions VIII and X, the EPA National Center for Environmental Assessment (NCEA), EPA Headquarters, the Coeur d'Alene Tribe, the Panhandle Health District, and the States of Montana and Washington. I also served on a sub-committee of the EPA Science Advisory Board evaluating the consistency of heavy metals regulation across EPA Program Offices in the early 1990s.

7. Based on that experience, IDHW-DOE requested that I participate on the advisory committee regarding development of the toxic air pollutant (TAP) rules for the State. As a result, I had a diverse perspective in the development of the TAPS rules that afforded reasonable health protectiveness while relieving the regulators and industry of the burden of the risk assessment and risk management protocols evolving at the time. I continued as DEQ BHSS lead risk assessor until 2014.

8. In my most relevant recent experience, I am working with the international humanitarian organization Médecins Sans Frontières (MSF, or Doctors Without Borders) assisting the Kyrgyz Republic Ministry of Health in developing health protective strategies to reopen both mercury and antimony smelters in Batken, Kyrgyzstan. These facilities were among the largest mercury and antimony producers in the former Soviet Union and are essential to the regional economy.

9. TIFO is currently engaged with MSF, the U.S. Department of State, the Massachusetts College of Pharmacy and Health Sciences, and the Kyrgyz Ministry of Health in conducting risk assessment and risk mitigation activities in active and abandoned Kyrgyz antimony and mercury mining communities. Biological monitoring of the local populations indicates many children and reproductive aged women have arsenic and antimony blood and urine levels exceeding international norms. The principal source of metals contamination are mining-related fugitive dusts contaminating the community water, soil, air, and food sources.

10. I am the lead risk assessor for these projects and have produced several major reports in the last five years. The project is currently engaged in implementing medical, environmental, public health advocacy and educational interventions to reduce exposures and health risks. As such, I have considerable insight and experience with the issues associated with the proposed antimony-gold operation at Stibnite.

11. Over the past five years, I have monitored the development of the U.S. Forest Service Draft Environmental Impact Statement (DEIS) for the Stibnite Gold Project (SGP) and have reviewed and submitted comments regarding the several revisions of the Draft Permit to Construct (PTC) and associated support documents. As a result, I am familiar with the many

related issues, and particularly those related to contaminants of potential human health and environmental toxicity concerns.

ASSIGNMENT

12. My understanding is that the Board of Environmental Quality has remanded the PTC to the Hearing Officer for additional consideration of DEQ's analyses of ambient air arsenic and carcinogenic risk issues. The Petitioners in this case have requested that I provide an expert opinion regarding the Board of Environmental Quality conclusions and the Respondent's and Intervenor-Respondent's Declarations. I understand the purpose of my opinion is to assist the Hearing Officer regarding additional factual evidence on the ambient air concentration analysis performed by DEQ for the PTC analysis.

DOCUMENTS REVIEWED

13. For this assignment, I have reviewed the transcript of the May 1, 2024 special meeting of the Idaho Board of Environmental Quality in the matter of Air Quality Permit to Construct Issued to Perpetua Resources Idaho, Inc. (agency case number 11 0101-22-01)[2], the May 9, 2024 FINAL ORDER FROM THE BOARD, Case Docket No. 010-22-01 OAH Case No. 23-245-01 (Final Order in the Matter of Air Quality Permit to Construct P-2019.0045)[3], the subsequent May 23, 2024 Memorandum in Support of Joint Motion for Reconsideration and/or Clarification of Final Order,[4] the subsequent June 12, 2024, ORDER ON PETITIONS FOR RECONSIDERATION AND/OR CLARIFICATION OF FINAL ORDER[5], and the July 8, 2024 Scheduling Order.[6]

[2] TR 0156.
[3] REC 3695.
[4] REC 3731.
[5] REC 3835.
[6] REC 3867.

14. I have also reviewed the two DEQ Respondent Declarations and attached materials: EXPERT DECLARATION OF KEVIN SCHILLING and EXPERT DECLARATION OF NORKA E. PADEN, Ph.D., two Perpetua Intervenor-Respondent Declarations and attached materials: EXPERT DECLARATION OF KEVIN LEWIS and EXPERT DECLARATION OF THERESA LOPEZ, and the Petitioner Declaration and attached materials: DECLARATION OF WILL TIEDEMANN.

SUMMARY OF CONCLUSIONS

15. I have reviewed Idaho Board of Environmental Quality's Final Order and understand and agree with the Board's conclusions that:

a. DEQ Did Not Act Reasonably and in Accordance with Law When it Analyzed the Ambient Arsenic Air Concentrations for the SGP;

b. DEQ did not Act Reasonably in Using a Five-Year Rolling Average for T-RACT that was not Properly Supported by Permit Conditions;

c. There was Insufficient Evidence to Support the T-RACT Analysis Limiting the Non-West End Pit Production Limit; and

d. DEQ Did Not Act Reasonably and in Accordance with Law When it Applied the 16/70 Calculation to the Ambient Arsenic Air Concentration Analysis.

16. I have reviewed the transcript of the May 1, 2024 special meeting of the Idaho Board of Environmental Quality. I also concur with Vice Chair McMillan's testimony that:

> . . . DEQ has misinterpreted how the acceptable ambient concentration for carcinogens, the AACC, must be applied if it is to comply with our air quality rules.
>
> … DEQ's creation and application of a project-specific adjustment factor is not supported by Idaho's air quality rules.

> … the creation of a project-specific adjustment factor suggests that there is a significant ignorance about cancer, carcinogens, and carcinogenesis.
>
> … the short-sighted project-specific adjustment factor to the Stibnite Gold Project, DEQ created a misleading risk analysis that greatly underestimates the actual cancer risk.[7]

17. This report supports the Board of Environmental Quality's findings in the Final Order and concludes that:

a. DEQ's application of the 16/70 SGP Project-specific adjustment factor underestimates cancer risk and is inappropriate science and public health policy;

b. Ambient air arsenic concentrations and cancer risk are underestimated for the SGP by use of 5-year rolling average in the air quality modeling input factors;

c. Ambient air arsenic concentrations and cancer risk are underestimated for the SGP by improper application of the non-WEP emissions scenario;

d. The combined application the SGP 16/70, 5-year rolling average, and non-WEP Project-specific adjustment factors increase cancer risk and negate the health protectiveness of the TAPs rule; and

e. DEQ's SGP Project-specific adjustment factors represent a significant change in the regulation of carcinogenic risk in Idaho that increases both cancer risk and regulatory burden.

[7] TR 0159.

OPINIONS

A. DEQ's application of the 16/70 Project-specific adjustment factor is inappropriate science and public health policy.

18. DEQ has failed to properly implement Section 586 and T-RACT for the SGP PTC by introducing a 16/70 SGP Project-specific adjustment factor to allocate the full 70-year lifetime allowable cancer risk to the 16-year Life of Mine (LOM). The calculation averages the risk resulting from SGP emissions over the life of the receptor. This adjustment allows the SGP to emit as much as 70 years of allowable carcinogenic emissions in 16 years. This type of "adjustment factor," also known as risk amortization or cancer dose-averaging, undermines both the health protectiveness and the regulatory certainty of the TAPs rule. In the context of the existing TAPs rule, as applied the last 30 years, using the 16/70 Project-specific adjustment factor is an incorrect interpretation and represents unsound science and public health policy.

19. Specifically, DEQ misinterprets the purpose and function of the **maximum one-year annual average ambient air carcinogen concentration** in implementing the TAPs rule. It is important to review the development of the TAPs rule in understanding the strategy represented by this one-year annual standard. The Schilling Declaration asserts that the TAPs rule was developed nearly thirty years ago to accommodate DEQ's predecessor agency IDHW-DOE and the regulated communities' request to adopt rules that are: 1) are reasonably protective of public health, but still afford flexibility to facilities and projects; 2) are relatively easy to understand and implement; and 3) do not require excessive expenditure of time and resources by DEQ and the permittee during the permitting process.[8]

[8] Schilling Decl. ¶ 13.

20. I was invited by the IDHW-DOE Air Quality Bureau to engage in development of those rules at that time in an advisory committee role based on my previous experience outlined above. My recollection is that much of the IDHW-DOE's and regulated industries' initial experience with risk assessment analyses was in implementing Risk Assessment Guidance for Superfund at CERCLA sites.[9] Both IDHW-DOE and the regulated community were supportive of avoiding the onerous burden of incorporating similar risk assessment and risk management protocols into Idaho's TAPa rule. In short, after considerable effort, IDHW-DOE was successful in developing the Section 586[10] and T-RACT[11] rule with a strategy that simultaneously avoids requiring PTC applicants to submit risk assessment and risk management protocols, yet is protective of human health.

21. The resultant TAPs Section 586 and T-RACT rules are highly prescriptive. Strict adherence to the rules is requisite to simultaneously afford regulatory certainty and simplicity for the regulated community and provide health protectiveness to the public. The key aspects of the simple, yet protective, rules are: 1) the incremental nature of the rule relieves industry and DEQ of the burden of assessing multiple sources and exposures, and greatly simplifies the permitting process; and 2) a significant **margin of safety (MOS)** is provided to ensure surrounding communities are not subjected to industry-generated ambient air TAP concentrations exceeding health-based risk criteria.

22. The purpose and function of the MOS is to protect the community from those other sources and exposures, risk cofactors, and uncertainties that would otherwise be evaluated in comprehensive risk assessment and health impact analyses. The DEQ and the regulated

[9] Exhibit B. U.S. EPA, *The Risk Assessment Guidelines of 1986* (Aug. 1987).
[10] IDAPA 58.01.01.586.
[11] IDAPA 58.01.01.210.12.

community have successfully employed these TAPs rule in a productive and protective manner since the 1990s.

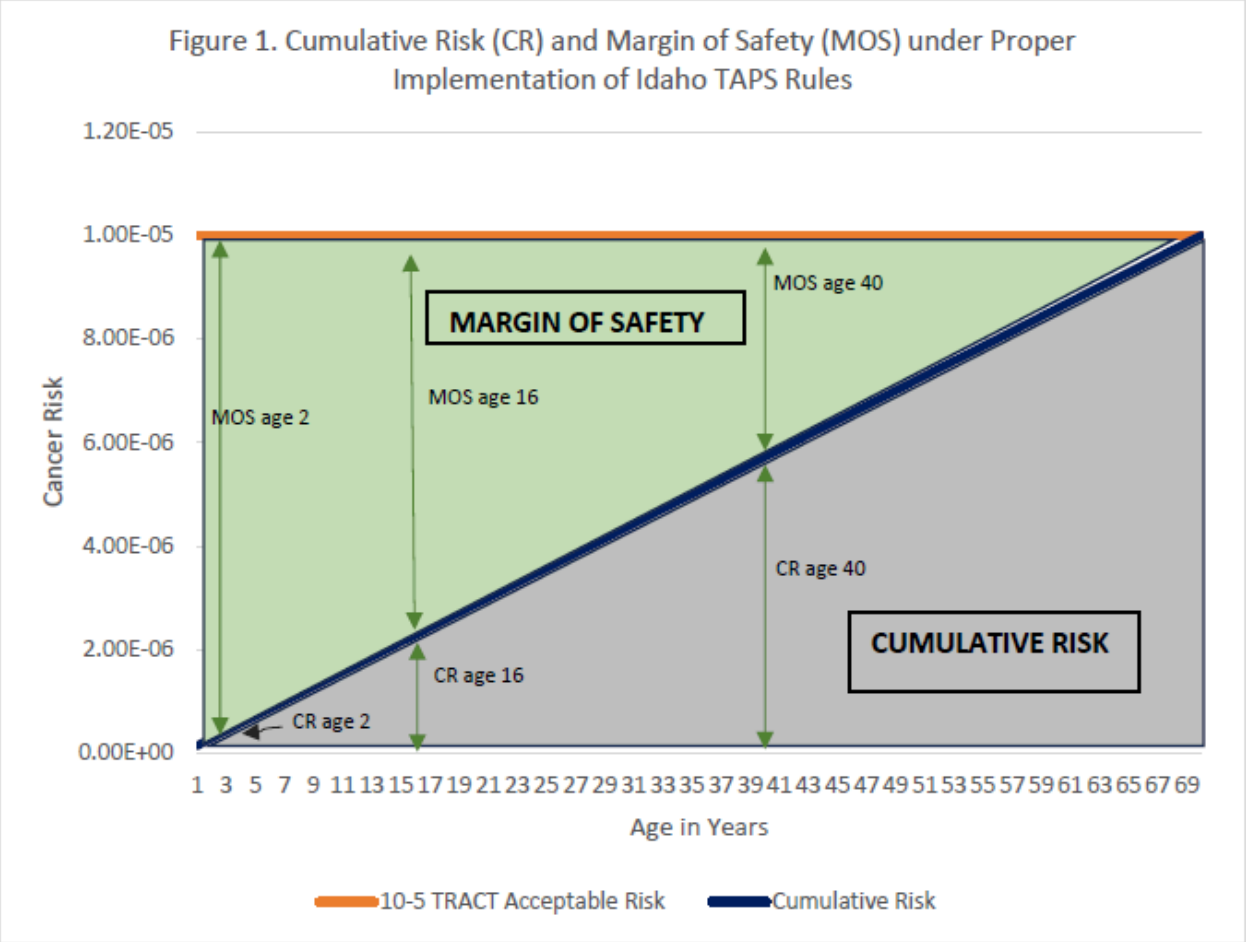
23. This prescriptive strategy specifically depends on protecting the public air space against the potential one-year annual maximum TAP emissions scenario throughout the life of the project. The one-year maximum emissions scenario is used to estimate **the maximum one-year annual average ambient air carcinogen concentration**. Ensuring that the maximum one-year annual ambient air carcinogen concentration does not exceed the acceptable ambient concentration for carcinogens (AACC) at the critical receptor location ensures that no receptor will be exposed to greater than the AACC by the incremental TAPs source for any year. The AACC is provided in Section 586 and is the ambient air concentration determined by dividing $1x10^{-5}$ lifetime risk by the Unit Risk Factor (URF). The URF is the lifetime cancer risk per 1.0 $\mu g/mg^3$ ambient air. Section 586 defines the AACC as an annual average.[12]

24. Ensuring that the criteria is achieved every year of the project guarantees the MOS will protect the individual receptors from other potential sources of the carcinogen that are not addressed in the incremental PTC analysis. Applying these criteria and MOS collectively to all individual sources assures that these health protections extend statewide.

25. Figure 1 illustrates the MOS and the cumulative lifetime risk at the critical receptor expected under the prescribed TAPS Section 586 maximum annual ambient concentration. The vertical axis is the carcinogenic risk. The horizontal axis represents the critical receptor's age commencing at the introduction of the incremental TAPs source. The

[12] *See* IDAPA 58.01.01.586 ("The AACC in this section are annual averages.").

maximum allowable lifetime risk is shown as the horizontal line at the top of the Figure ($1x10^{-5}$ T-RACT risk in this example).



26. If the TAPs rule is properly implemented, the cumulative incremental risk is shown by the diagonal line proceeding from birth to age 70 years (i.e., risk is allowed to accumulate at an annual rate of $(1x10^{-5})/70$ per year, or (AACC*URF/70) under T-RACT. The gray area below the diagonal line represents the portion of allowable lifetime risk accumulating from the incremental source. Risk increases proportional to the receptor age and the individual will have received the full allowable lifetime T-RACT exposure, and have a 10^{-5} carcinogenic risk burden at age 70-years.

27. The green area above the diagonal line represents the margin of safety (MOS) for the receptor to accommodate other contaminant exposures, risk cofactors, or uncertainties that might increase cancer risk from sources other than the incremental emissions regulated under TAPs Section 586 and T-RACT. Specifically, the large MOS safely accommodates those risk considerations that would otherwise be addressed in onerous risk and health assessment protocols. In this manner Idaho's TAPs compliance strategy purposefully, but safely, avoids requiring risk analyses.

28. The strategy also extends maximum protection to those population sub-groups most sensitive to carcinogenesis. Important life-stages of the receptor are indicated by the vertical lines at ages 0-2 years for infants and toddlers, ages 3-16 for children and adolescents, ages 17- 40 for reproductive-aged women and the fetus, and ages 41-70 years for older adults. This Idaho TAPs rule strategy affords minimal cumulative risk and maximal MOS protection during early life stages and pregnancy, acceptable risk levels during most of adulthood, with lesser protection at advanced ages when incremental cancer risk has limited effect on lifetime cumulative risk.

29. In the case of arsenic under the T-RACT criteria, the allowed annual rate of risk accumulation is a direct function of the .0023μg/m^3 T-RACT AACC multiplied by URL/70. As a result, contrary to Respondents' assertions, the AACC functions as an annual standard as historically applied in the TAPs rule. DEQ's and Perpetua's Declarations contend the Section 586 comparison of average annual ambient air arsenic concentration should utilize the average 70-year concentration, as opposed to basing health protectiveness on the worst-case **maximum one-year annual average ambient air carcinogen concentration** that is the foundation of the

MOS. Using the 70-year basis proposed by DEQ and Perpetua allows Perpetua to emit a lifetime of allowable emissions in 16 years, and undermines the health protectiveness of the rule and increases cancer risk.

30. The origin of DEQ's policy change can be found in the Lewis and Schilling Declarations. The initial Draft PTC offered by DEQ for public review exempted 99% of proposed allowable arsenic emissions from regulation and TAPs compliance because mining fugitive dust was not considered. Following subsequent public hearing testimony, DEQ required that Perpetua consider haul road dust arsenic emission under Section 586 TAPs rule.[13] As Schilling asserts, when subsequently required to consider the massive arsenic emissions, Perpetua informed DEQ that compliance with either the 10^{-6} AACC or the 10^{-5} T-RACT AACC limits were not achievable.[14] Any calculations or analyses to support these conclusions have never been disclosed.

31. According to Schilling, DEQ then suggested the ad hoc SGP 16/70 Project-specific adjustment factor, or dose-averaging approach, to avoid the annual one-year average constraints of the TAPs rule.

> Rather than revise the analytical approach to provide a less conservative assessment of impacts, I proposed that compliance with carcinogenic TAP increments could be based on cumulative cancer risk of the limited-duration project rather than the worst-case annual impact for a project of limited duration.[15]

32. The SGP 16/70 Project-specific Adjustment Factor was introduced in the TAPs Modeling Addendum, Section 4.3 AACC Adjustment for the Operational Life of the Mine.

[13] Lewis Decl. ¶ 18.
[14] Schilling Decl. ¶ 22.
[15] Schilling Decl. ¶ 22.

> [Perpetua] indicated the maximum life-of-mine will be 16 years. Life-time exposures to carcinogenic TAPs were refined by multiplying the maximum modeled annual impact by a ratio of 16/70.[16]

33. In defending this policy change, Schilling asserts that DEQ's position that the short-term factor of 10 applied to the allowable AACC when a project will have a duration of less than 5 years, shows that an adjustment in the exposure concentration is appropriate.[17] He further asserts that:

> . . . DEQ determined it would not be appropriate to subject individuals to a lifetime allowable cancer risk within a duration of less than 5 years. Therefore, the adjustment was capped at 10, rather than using a higher value or values calculated from exposure durations of 5 years of less (e.g., 70 years/5 years = 14 or 70 years/2 years = 35). These short-term projects were most commonly remediation and pilot-scale projects having a duration of up to several years.[18]

34. Schilling refers to IDHW-DOE's explicit 1992 interpretation,[19] also noted by Lopez,[20] that:

> For short term sources (usually less than five years in duration), such as remediation projects, a probability of greater than one in a million risk (over 70 years) will generally be acceptable to account for the decreased term of exposure. It is not acceptable however, for exposed individuals to receive a full 70-year exposure during the life of a short-term project. (Idaho DEQ 1992).[21]

35. In my opinion, nothing in the 1992 IDHW-DOE document suggests that an "adjustment factor" can be applied to any project with a life greater than 5 years, as the Schilling and Lopez Declarations imply is the modified DEQ policy. I am not aware of any quantitative

[16] REC 0698.
[17] Schilling Decl. ¶ 19.
[18] Schilling Decl. ¶ 19.
[19] Schilling Decl. ¶ 19.
[20] Lopez Decl., Memo. in Supp. of Decl. at 11.
[21] REC 3780.

"adjustment factor" connection between the 5-year project lifetime and the 70-year lifetime cancer risk basis. I believe that it is more accurate to describe the short-term factor of 10 as reflecting the order of magnitude increase in allowable risk from 10^{-6} to 10^{-5} criteria. This order-of-magnitude relief in allowable risk levels is commonly justified in cancer risk mitigation protocols throughout State and federal jurisdictions in various programs for various reasons, such as the Washington State protocols.[22]

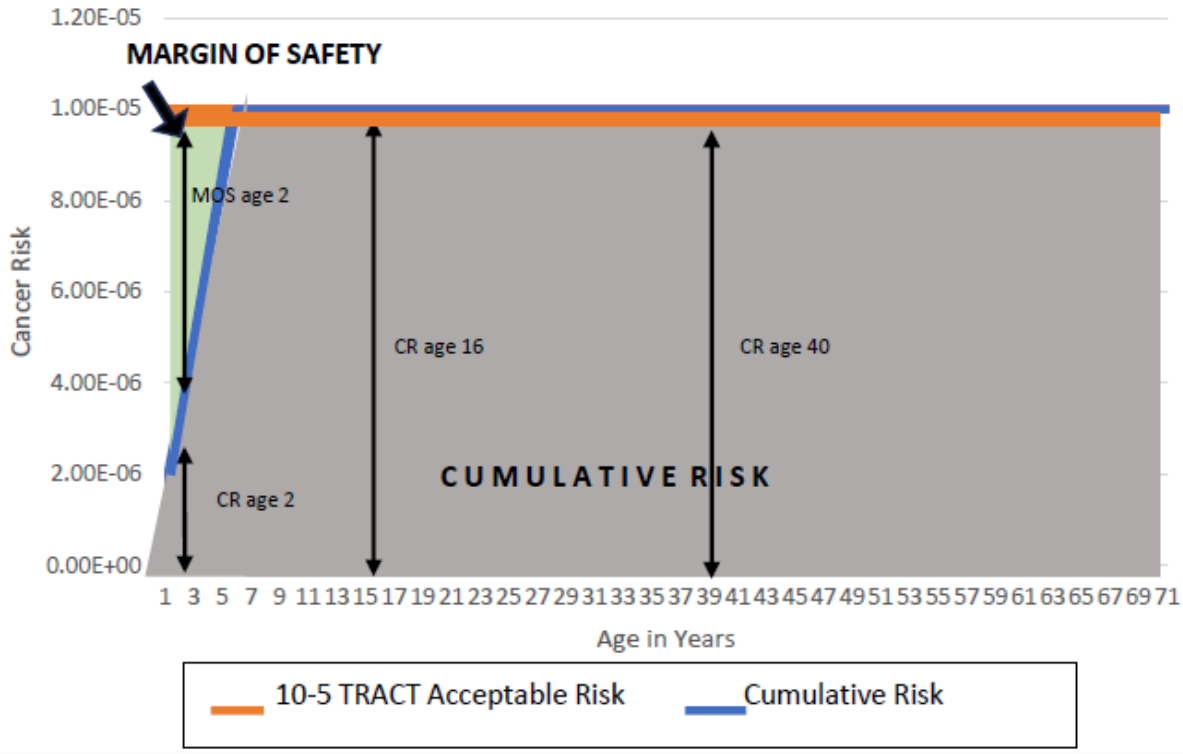
36. According to Schilling and Lopez, DEQ's modified policy implies that the SGP Project-specific adjustment factor can be applied to any carcinogenic source with a duration greater than five years. This shortsighted conclusion is incorrect, unprecedented, and not supported by EPA guidelines. The new policy is poor science and undermines the health protective strategy of regulating TAPs that has successfully been applied for the last thirty years.

37. Consider the extreme case of DEQ permitting a six-year (>5 yr.) life facility to emit sufficient carcinogens to expose individuals to the full 70-year lifetime acceptable risk in six years. The alleged allowable maximum annual ambient concentration would be 70/6 = 11.7 times the AACC, (or 117 times the AACC if T-RACT applied, (i.e. 1.17×10^{-4} cancer risk if applied for 70 years). DEQ's misinterpretation would allow emissions and consequent exposures of more than two orders of magnitude greater risk than the AACC (1.2×10^{-4} equivalent risk) for six years. At year 7 (or 10% of the receptor's assumed lifetime), the six-year-old child will have accumulated, and carry the lifetime burden, of a one-in-one hundred thousand cancer risk (10^{-5}). This risk burden will accompany the individual for the following six decades (> 90%) of the receptor's expected lifetime.

[22] Exhibit C. Washington State Department of Ecology, *Guidance Document First, Second, and Third Tier Review of Toxic Air Pollution Sources (Chapter 173-460 WAC)* (2010).

38. The effect of this dangerous scenario is illustrated in Figure 2. The MOS afforded this childhood receptor occurs briefly in the first six years of life. For the remainder of the receptor's lifetime, any additional arsenic exposure, from any source at any time, would immediately cause the cumulative lifetime exposure to exceed the unacceptable $>10^{-5}$ risk. The receptor would be challenged to avoid any additional arsenic exposures for the remainder of life.

Figure 2. Cumulative Risk (CR) and Margin of Safety (MOS) using the Project-specific (6/70) Adjustment Factor for a 6-year project



39. The ad hoc introduction of risk averaging by DEQ through a 6/70 adjustment factor, as depicted in Figure 2, would allow a six-year project to concentrate 70 years of emissions and lifetime cancer risk into both the 6-year life of the project and receptor child's first

six years of life. This scenario undermines the health protectiveness originally incorporated in Section 586, particularly with respect to neo-natal, pediatric, and adolescent cancers.

40. In justifying the use of the 16/70 Project-specific adjustment factor, the Respondents continually assert that the Unit Risk Factor (URF) is an average based on a 70-year lifetime. However, carcinogenic potency and cancer risk accumulation differ for various stages of life. The cancer dose varies based on contaminant intake and absorption rates and physiological factors such as body weight and organ development. Considering early life exposures, warrants additional examples of the inappropriateness of introducing the SGP 16/70 Project-specific adjustment factor. Pregnant women, the fetus, and pre-school children accumulate dose and risk at the highest rates and are especially vulnerable to disease due to age and developmental factors. Body weight, absorption, and hormonal considerations can make older children and adolescents more susceptible to childhood cancers.

41. DEQ's assertion that the SGP 16/70 Project-specific adjustment factor is health protective implies that it is permissible to subject these sensitive subpopulations to the equivalent $>10^{-4}$ risk levels from conceptus to school age because it will average out over the remainder of the child's life.

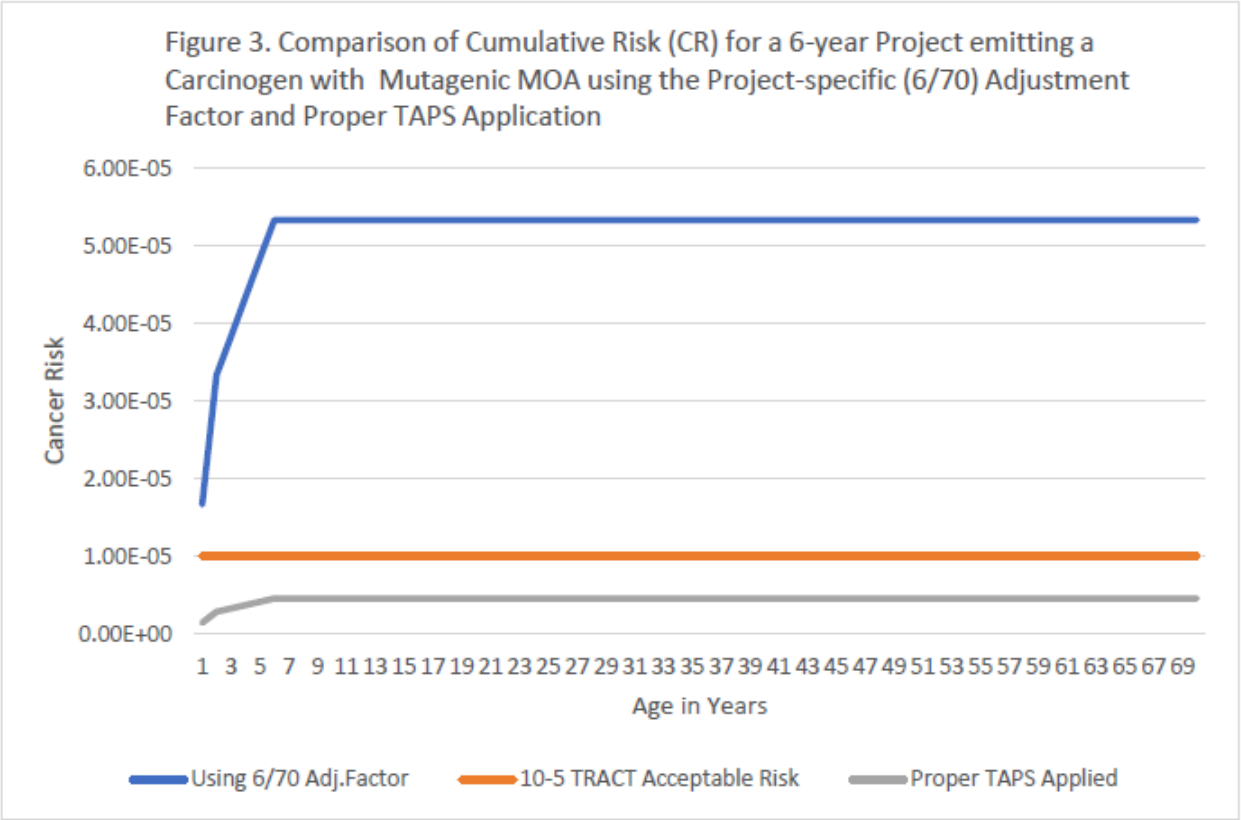
42. The SGP 16/70 Project-specific adjustment factor is a classic example of dose-averaging. The practice of averaging cancer risk over a receptor's lifetime progressively developed as an issue in the risk analyses applied to contaminated hazardous waste sites during the 1990s, and early 2000s. The EPA comprehensively considered the application of

dose-averaging or risk amortization in the Science Advisory Board (SAB) review *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens.*[23]

43. The excessive risk associated with early life-stage carcinogenic dose accumulation has long been recognized by most health authorities and specific protections were incorporated in EPA Risk Assessment Guidance for Superfund (RAGS) policy in 2009. The EPA recommends a quantitative adjustment of the toxicity value to account for early life susceptibility. This guidance recommends a 10-fold adjustment for exposures during the first 2 years of life; 3-fold adjustment for exposures from ages 2 to <16 years of age for carcinogens exhibiting mutagenic mode of action (MOA).[24]

44. Figure 3 shows lifetime cumulative risk were DEQ to apply the ad hoc 6/70 adjustment factor to a carcinogen exhibiting mutagenic MOA for the 6-year project life scenario (blue line). Applying the recommended age-specific adjustment factor shows that DEQs interpretation allowing dose-averaging over the 70-year lifetime would result in the allowable full lifetime exposure occurring by age 2 years, and the child's lifetime cumulative exposure will be $5.3x10^{-5}$ by age 6 (i.e., 53 times the one-in-one million criteria). These lifetime cumulative risks acquired by infants and toddlers, prior to adolescence far exceed EPA acceptable carcinogenic risk policy.

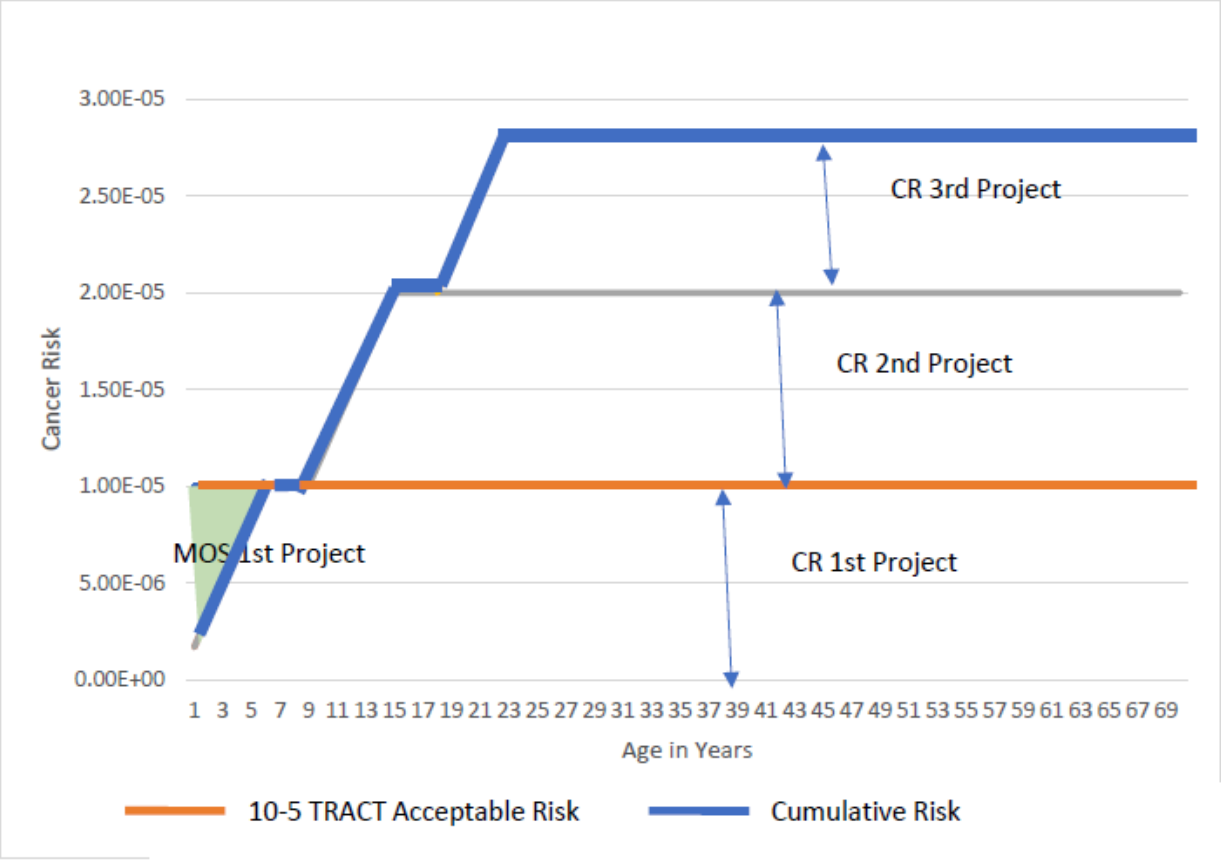
[23] Exhibit D. U.S. EPA, *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (2005).
[24] Exhibit E. U.S. EPA, *Risk Assessment Guidance for Superfund. Vol. I: Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment* (Jan. 2009).



45. Conversely, proper application of the TAPs rule using the **maximum one-year annual average ambient air carcinogen concentration** is shown by the lower cumulative risk line (gray line). Proper implementation of the TAPs rule would result in 4.6×10^{-6} cumulative cancer risk at age six years, as shown in Figure 3. These results demonstrate that application of a 6/70 adjustment factor for a six-year facility increases a six-year-old child's cancer risk by 12 times over that were the TAPs rules applied under the past policy.

46. As another example, consider the case of two additional 6-year projects being implemented near the source represented in Figure 2 at years 9 and18 in this child's life. Figure 4 shows the child already exposed to the full lifetime allowable cancer $1x10^{-5}$ risk by age 6, will have double ($2x10^{-5}$) the acceptable risk level by adolescence, and will carry three times the allowable lifetime cumulative risk burden ($3x10^{-5}$) through the reproductive stage of life.

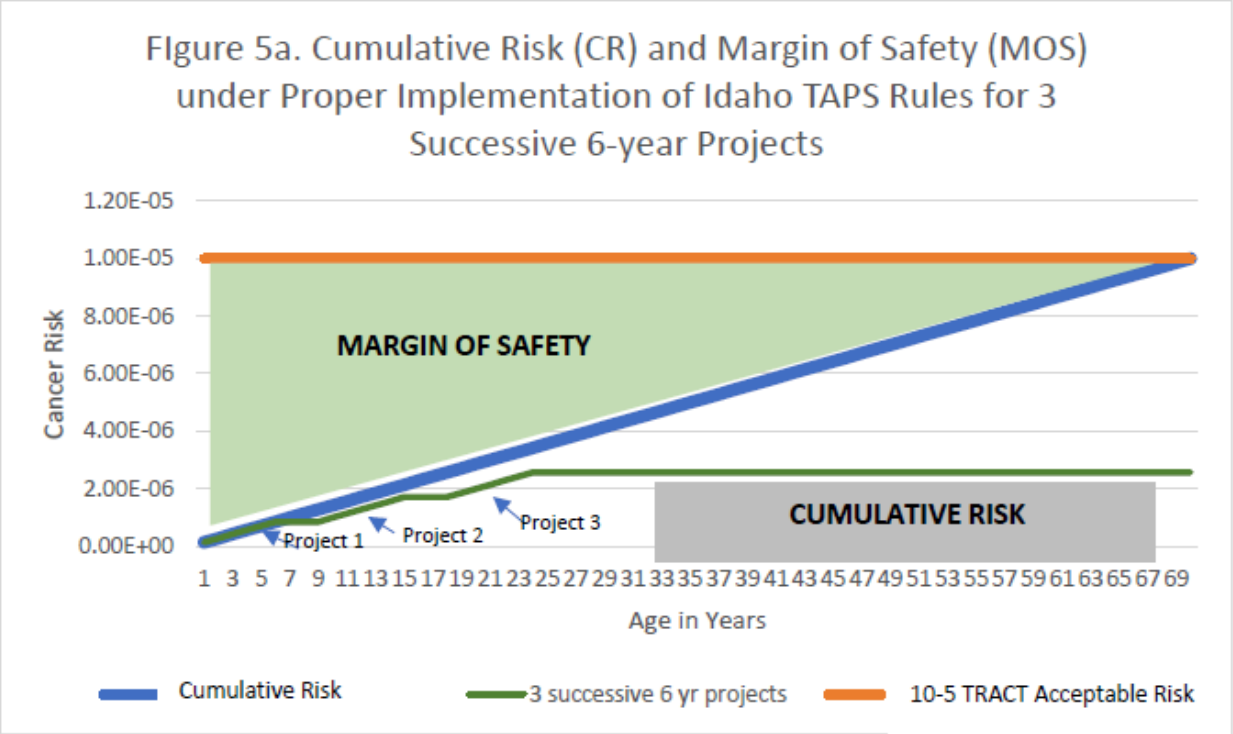
Figure 4. Cumulative Risk using the Project-specific (6/70) Adjustment Factors for 3 Successive 6-year Projects



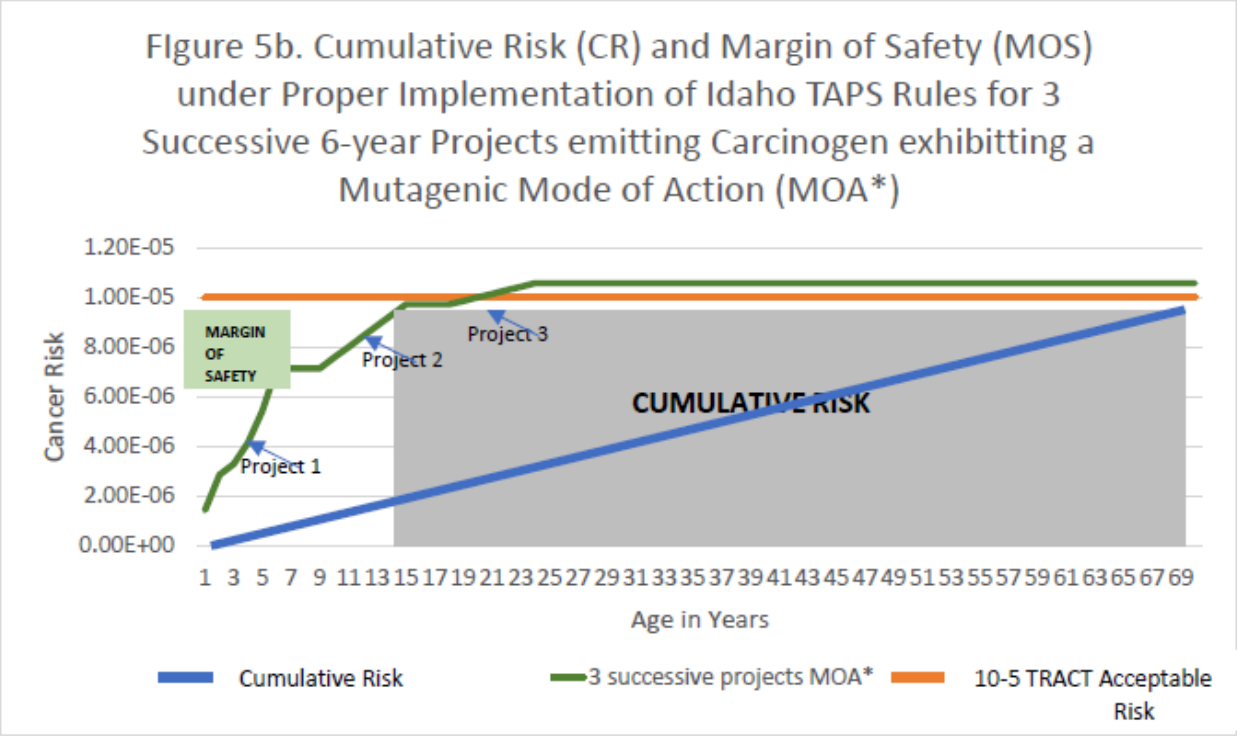
47. Consider the three sequential 6-year projects implemented under the new (6/16) adjustment factor emitting a carcinogen exhibiting mutagenic MOA. In this scenario, the three projects would increase individual cancer risk to $>1x10^{-5}$ lifetime allowable risk by age 2, to $5.3x10^{-5}$ for a 6-year-old child, $8.3x10^{-5}$ for a 16- year old adolescent, and $9.3x10^{-5}$ for a 24-year old adult. These are dangerous and unacceptable risks at vulnerable life stages.

48. Under Section 586, DEQ must consider these new projects incrementally. Thus, it would not account for the cumulative lifetime exposures associated with the earlier projects in a new source PTC application, and are not allowed to consider risk associated with those earlier projects. At Stibnite, for example, should SGP apply to open another pit at the mine, DEQ would be required to ignore the cumulative lifetime risk and cancer burden imposed by the proposed SGP 16-year LOM scenario.

49. Figures 5a and 5b demonstrate the same three sequential project scenarios under the proper implementation of the current TAPs rules using the **maximum one-year annual average ambient air carcinogen concentration** that incorporates the MOS to accommodate additional sources. Figure 5a shows the cumulative risk from all three projects for a carcinogen not exhibiting mutagenic MOA. In this case, a child growing up in the community would be protected from excess cancer risk through all life stages even though DEQ would not consider the earlier exposure in applying Section 586. The lifetime risk accrued by the individual is $2.6x10^{-6}$ as opposed to $3.0x10^{-5}$ in the earlier example. Allowing use of the 6/70 adjustment factor increases lifetime cancer risk by 12 times..



50. Figure 5b shows the cumulative risk for proper implementation of the current TAPs rule for three sequential 6-year projects emitting a carcinogen exhibiting mutagenic MOA. In this example, the MOS is successfully protective throughout childhood and adolescence, with the cumulative risk exceeding the 10^{-5} risk level at age 21. These examples illustrate the effectiveness of the MOS in accommodating additional sources and risk cofactors. The TAPs rule is health protective if properly implemented. Applying risk averaging through the use of the 16/70 Project-specific adjustment factors eliminates the MOS and substantially increases cancer risk, especially considering the incremental nature of the rule.



51. Figures 5a and 5b also demonstrate DEQ's shortsightedness in applying unprecedented cancer dose-averaging methods through the SGP 16/70 Project-specific adjustment factor. The inappropriate averaging is allegedly justified by ad hoc risk assessment calculations and risk management protocols that undermine both the simplicity and the health protectiveness of the TAPs rule. The MOS is compromised, the public is no longer secure, and the regulated industry is now obliged to include cancer risk and health impact assessments in TAPs PTC applications to support the assertions of health protectiveness.

52. There are no provisions in the Air Rules to allow manipulation of the required **maximum one-year annual average ambient air carcinogen concentration** or the **AACC,** or to submit risk calculations. The Respondents assert that because there are no specific prohibitions, using the SGP 16/70 Project-specific adjustment factor is permissible. DEQ did not

require any risk assessment justification during the PTC process, but only provided extremely limited risk analyses in post hoc declarations following the Special Board Hearing.[25]

53. In justifying the SGP Project-specific 16/70 adjustment factor, both the DEQ and Perpetua refer to the EPA Risk Assessment Guidance for Superfund (RAGS) risk assessment protocols eschewed by the agency for the last thirty years to support the ad hoc exposure averaging calculations. As noted in the Tiedeman Declaration, IDHW-DOE specifically avoided RAGS waste site remediation short-term risk protocols in developing the TAPS.[26]

54. The Board of DEQ Vice Chairman McMillan explicitly expressed concerns with this issue, indicating his belief that DEQ's creation and application of a Project-specific adjustment factor cannot be supported by Idaho's Air Rules and that DEQ has misinterpreted how the AACC must be applied if it is to comply with the those rules.

55. Vice Chairman McMillan further indicated that DEQ's application of what he called the "short-sighted" Project-specific adjustment factor to the Stibnite Gold Project created a misleading risk analysis that greatly underestimates the actual cancer risk. In his view:

> The Idaho rules are not ambiguous. There is an acceptable risk associated with the AACC standard. There is an acceptable risk associated with DEQ-approved T-RACT projects, and there is an acceptable risk associated with the short-term project that is five years or less. There are no other acceptable risks identified in Idaho's air quality rules.[27]

I agree with Dr. McMillan's statement.

[25] *See* Schilling Decl.; Paden Decl.; Lewis Decl.; Lopez Decl.
[26] Tiedemann Decl. ¶¶ 26-27.
[27] TR 0160.

B. Ambient air arsenic concentrations and cancer risk are underestimated for the SGP by using a 5-year rolling average in the air quality modeling input factors.

56. Another ad hoc SGP Project-specific adjustment factor DEQ applied to the exposure estimates (prior to implementing the 16/70 Project-specific adjustment factor) was a 5-year rolling average adjustment factor to the emissions rates used as input to the refined modeling. This disguised risk averaging technique results in the models predicting a five-year average ambient air carcinogen concentration rather than the **maximum one-year annual average ambient air carcinogen concentration** required under Section 586 and T-RACT, further undermining the health protectiveness of the TAPs rule.

57. The 5-year rolling average adjustment factor was introduced in the TAPS Modeling Addendum Section 4.2 -TAP Emission Averaging Period. In Section 4.2, DEQ asserts:

> Annual average emissions of carcinogenic TAPs are typically used in the dispersion model to estimate maximum annual impacts. PRI refined the analyses by using source-specific emission rates that are representative of a 5-year averaging period. This approach is appropriate because carcinogenic impacts are of concern from a long-term exposure basis.[28]

58. DEQ erroneously substitutes the 5-year rolling average emissions for the maximum one-year potential emissions required under Section 586 and T-RACT. Section 586 requires the prescribed maximum one-year annual average to be estimated by refined modeling of ambient concentrations based on maximum one-year potential emission rates, or PTE. The PTE should reflect the source configuration and operational scenario that would yield the maximum annual one-year ambient air arsenic concentration. This concentration is then

[28] REC 0698.

compared to the 10^{-6} AACC. If the 10^{-6} AACC is exceeded, the applicant may apply for 10-fold relief under TRACT.

59. DEQ has never disclosed this comparison. In response to public comments critical of DEQ for not calculating nor presenting the required AACC comparisons, DEQ provided the following rationale:

> The comparison offered, comparing maximum annual impacts to the T-RACT adjusted AACC, is irrelevant. Compliance with TAPs rules was demonstrated through a refined analysis, so there is no utility in focusing on results from a more conservative, less refined analysis.[29]

DEQ misinterprets the purpose the comparison and undermines the health protective strategy of the TAPS Rules as implemented in the past.

60. Instead, DEQ substituted the 5-year rolling average for the required maximum one-year emission rate. There is no provision in the TAPs rule for altering or adjusting the predicted maximum one-year annual average. This erroneous substitution significantly reduces the MOS inherent in proper allocation of the one-year maximum emission rates. To be health protective, the prescriptive Section 586 rule explicitly (not typically) requires predicting the **maximum one-year annual average contaminant concentration** using prescribed emissions estimates, and assuring that concentration is not exceeded during the life of the facility.

61. DEQ has never disclosed the required **maximum one-year ambient annual average arsenic concentration.** It is not possible from the available information provided by DEQ to determine how this 5-year rolling average compares to the maximum one-year emission rate that should have been used. I have estimated the underprediction by examining the ratio of

[29] REC 0693.

peak to mean 5-year rolling average emission rates presented in Figure 3 of Perpetua's TAP Addendum.[30] This figure shows estimated potential 5-year rolling average emissions for an alleged 16-year MODPRO2 operations plan. The estimated mean 5-year rolling average from this figure was calculated to be 0.132 lb/hr. Comparing this value to the maximum 0.232 lb/hr value suggests the peak to mean ratio for the alleged T-RACT PTE is approximately 1.8 (0.232 lb/hr / 0.132 lb/hr).

62. Because this Project-specific 5-year rolling average adjustment factor is inherently applied to the emissions input to the refined models, a 1.8 underprediction factor would translate directly to the estimated receptor point ambient air carcinogen estimates. As a result, the maximum one-year annual concentration in the model output is likely underpredicted by a factor of 1.8. The best estimate of the **maximum one-year annual ambient air arsenic concentration** for the modeled scenarios is 0.0125 $\mu g/m^3$ (1.8 x 0.00698 $\mu g/m^3$) for the WEP2.[31]

63. DEQ's application of the 5-year rolling average adjustment factor reduces the **maximum one-year annual ambient air arsenic concentration** and the associated cancer risk by 45%.

C. Ambient air arsenic concentrations and cancer risk are underestimated for the SGP by improper application of the non-WEP emissions scenarios.

64. A third SGP Project-specific adjustment, the non-WEP adjustment factor, was applied to model predicted ambient air concentrations. This is a second disguised dose-averaging step combining eight different 5-year rolling average scenarios, reducing the alleged WEP2

[30] Exhibit L. at 26.
[31] Exhibit L at PDF 224.

maximum annual average an additional 41%. DEQ averaged the maximum WEP2 scenario 5-year average arsenic concentration predicted by the model (i.e. 0.00698 μg/m^3) with the average of the seven model predicted non-WEP 5-year average concentrations (0.00134 μg/m^3). These alleged annual averages are actually an average of 5-year averages as these were predicted by the already diluted 5-year rolling average emissions input to the refined modeling. This non-WEP multi-averaging adjustment factor dilutes the ambient air carcinogenic concentration by an additional 41%, yielding the 0.00416 μg/m^3 alleged incremental annual ambient arsenic concentration. Paden and Lopez use this value to assert compliance with EPA cancer risk policies in subsequent risk calculations.[32]

65. DEQ and Perpetua assert this additional dose-averaging step is justified because no one scenario will apply throughout the 16-year LOM operation. In the context of properly applying the TAPs rule, the non-WEP adjustment factor is irrelevant. DEQ's obligation is to identify the emission scenario that produces the **maximum one-year annual average ambient air carcinogen concentration**. That value is the maximum WEP2 scenario, and would not consider non-WEP scenarios unless the non-WEP emissions sources were operating contemporaneously during the WEP2 emission maximum year. In that case, any non-WEP scenario operating in the same year as the WEP2 maximum configuration would add to, not dilute, the critical receptor maximum ambient air concentration.

66. DEQs applying the SGP Project-specific non-WEP adjustment factor effectively converts the 5-year alleged annual average value (0.00698 μg/m^3) to an arbitrary 0.00416 μg/m^3 16-year LOM average carcinogenic concentration. A variety of combinations of the different

[32] *See* Paden Decl. XXX; Lopez Decl. XXX.

modeling scenarios, based on alleged operations plans could have been combined to manipulate this multi-averaged hybrid LOM ambient air carcinogenic exposure estimate (e.g. 3-year rolling average and 70% non-WEP contribution).

67. The final effect of DEQ's application of an arbitrary multi-averaging non-WEP adjustment factor can be estimated by comparing the WEP2 and non-WEP average ambient air carcinogen estimates (i.e., (0.00698 $\mu g/m^3$ / 0.00416 $\mu g/m^3$), or by a factor of 1.7. Applying the non-WEP Project specific adjustment factor underpredicts the required **maximum one-year annual average ambient air carcinogen concentration** and associated cancer risk by an additional 41%.

D. The combined application of the SGP 16/70 Project-specific adjustment factor, the 5-year rolling average adjustment factor, and the non-WEP adjustment factor increase cancer risk and negate the health protectiveness of the TAPs rule.

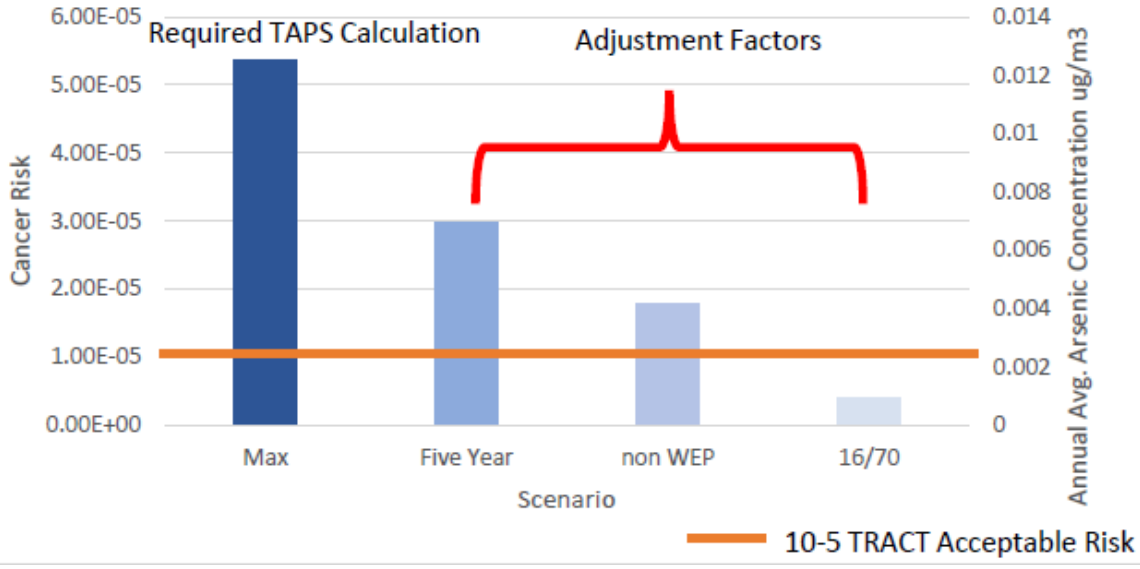
68. The conclusions in the DEQ Board's Final Order correctly identified the three Project-specific adjustment factors that undermine the health protectiveness of the TAPs rule for carcinogenic risk. The Board correctly concluded that application of these adjustment factors underestimates cancer risk. DEQ applied the: 1) 5-year rolling average; 2) non-WEP; and 3) SGP 16/70 LOM adjustment factors sequentially to the input and the output of the predictive air quality model. As a result, the dilution effects are multiplicative, rather than additive.

69. In summary, DEQ diluted the (0.0125 $\mu g/m^3$) maximum one-year annual average ambient air carcinogen concentration by 45% to 0.00698 $\mu g/m^3$ by applying the 5-year rolling average. DEQ further diluted 5-year average concentration by 41% to a value of 0.00416 $\mu g/m^3$ by applying the non-WEP adjustment factor, which is diluted an additional 78% to a value of 0.00095 $\mu g/m^3$ by applying the 16/70 SGP Project-specific adjustment factor. In total, DEQ

diluted the required **maximum one-year annual average ambient air carcinogen concentration** by 93%, or a factor of 13 times before calculating the corresponding cancer risk.

70. The risk levels associated with these exposures were similarly underpredicted as follows: the risk for estimated **maximum one-year annual average ambient air carcinogen concentration** of $5.3X10^{-5}$ was (1) diluted to $3x10^{-5}$ by applying the 5-year rolling average adjustment factor; (2) diluted to $1.8x10^{-5}$ by applying the non-WEP adjustment factor; and (3) to the alleged compliance $4x10^{-6}$ by applying the SGP 16/70 Project-specific adjustment factor. These results are shown in Figure 6. DEQs sequential application of the three SGP Project-specific adjustment factors underpredict cancer risk by 13 times, as these carcinogenic risk levels are employed in properly implementing the TAPs rule.

Figure 6. Effect of DEQs Application of the Project-specfic Adjustment Factors Compared to Required TAPS Calculation



71. These analyses confirm Vice-chairman McMillan's observation in the Special Hearing:

> The PTC proposes to allow 16 years higher daily carcinogen doses and disguises such doses using a non-rules-based mathematics.[33]

E. DEQ's SGP Project-specific adjustment factors represent a significant change in the regulation of carcinogenic risk in Idaho that increases both cancer risk and regulatory burden.

72. As DEQ admits,[34] cancer dose-averaging has seldom, if ever, been used in TAPs carcinogenic risk compliance evaluations for a stationary source under the Clean Air Act in Idaho. Although there is a history of using cancer dose-averaging in risk assessment and risk management protocols for short-term remediation projects at contaminated sites, applying it to the SGP PTC is unprecedented. In implementing the SGP 16/70 Project-specific adjustment factor, DEQ has deviated from the long-held prescribed TAPs rule protocol of guaranteeing the **maximum one-year annual average carcinogen concentration** will not exceed the AACC or T-RACT AACC for each year of the Project. This thirty-year health protective strategy has provided the public comfort that cancer risk exposures are within acceptable limits both near the source and Statewide.

73. Should application of risk averaging become precedent through acceptance of the SGP Project-specific adjustment factors, the conservative MOS inherent in the TAPs rule is significantly reduced. This major change in health protective strategy should simultaneously require PTC applications to include a comprehensive health risk assessment to consider other

[33] TR 0160.
[34] REC 1201.

potential sources otherwise inherently addressed in the MOS. Providing such evidence would be incumbent upon both the PTC applicants and DEQ.

74. These health and risk assessments would require new applicants to consider other past, present, and future sources that did, or may, expend significant portions of the critical receptor's lifetime allowable risk. A simple review of Washington State's required Health Impact Assessment (HIA) points out the numerous shortcomings in the ad hoc alleged risk analyses offered by the Respondents. The HIA requires specified emissions calculations, approved air dispersion modeling, AACC screening, risk assessment, hazard identification, exposure estimates considering other sources and exposure routes, dose-response criteria, non-carcinogenic risk characterization, uncertainty analysis, discussion of acceptability of risk, and a risk management analysis employing modified emission control strategies.[35]

75. DEQ has no history utilizing risk assessment to support TAPs rule applications, nor do the Idaho TAPs regulations offer any guidance for conducting health risk analyses. No comprehensive analyses, nor discussion related to risk and health assessment, are found in the Statement of Basis for the SGP PTC.[36] No comprehensive assessment of health and risk issues associated with application of the SGP Project-specific adjustment factors were required in Perpetua's application.

76. Additionally, from a regulatory standpoint, other Idaho air permit applicants may seek similar preferential relief. No facility plans for a 70-year life. The 70-year basis is an artifact of cancer risk analyses protocols, not a facility design criterion. Every facility ever to apply for a

[35] Exhibit C at 26.
[36] *See* REC 0410.

PTC that did not opt for short-term relief (less than 5 years) likely anticipated a project life of less than 70 years of operation. Will DEQ offer SGP-equivalent project-specific adjustment factor relief and require comprehensive Health Impact Analyses for 6/70, 10/70, 16/70, 20/70, 25/70, 30/70-year alleged project life, as Schilling Declaration suggests?[37] Will DEQ approve incremental emissions from a new source impacting the same critical receptor location that has already expended its lifetime allowable risk, as demonstrated in Figures 4 and 5, above? Will DEQ approve additional emissions from the same location after the original permit has exhausted the critical receptor lifetime allowable risk? Will DEQ require, and provide guidelines, for risk and health assessments to support the preferential relief?

77. These questions demonstrate the short-sightedness of DEQ's acquiescence to Perpetua in allowing dose-averaging concepts to be applied to the Section 586 TAPs rule. Proper application of the rule inherently precludes risk averaging to maintain health protectiveness, without requiring applicants to address the issues without guidance. The regulatory burden placed on future applicants by this modified policy is potentially immense.

78. Allowing Perpetua and the SGP to concentrate a lifetime of carcinogenic emissions and allowable risk in a shorter exposure period defined by the LOM introduces numerous issues and uncertainties that can appropriately be considered only in comprehensive risk assessment analyses.

79. There are numerous examples of inadequacies of the risk calculations offered by the Respondents. Among the more important are those related to the SGP Project-specific adjustment factors concentrating emissions and carcinogenic risk in childhood and adolescent

[37] *See* Schilling Decl. ¶ 19.

life stages. Environment Canada conducted an extensive review of the development and incorporation of life stage cumulative risk assessment, and particularly dose-averaging.[38]

80. This document provides an understandable and concise review of the several issues surrounding dose-averaging, and risk amortization in applying cumulative risk assessment to short-term exposure scenarios. The report also evaluates and describes how various U.S. and Canadian health agencies had implemented risk amortization policy in the preceding decade. Environment Canada's conclusions reflect earlier EPA's determinations that dose averaging generally underestimates risk for fetus, infant, toddler, school children and adolescents; can be appropriate for healthy adults; and overstates risk late in life.[39] Idaho's current TAPs rule MOS appropriately accommodates both these conclusions if properly implemented as illustrated in Figure 1, above.

81. Environment Canada's conclusion with regard to threshold carcinogens is most pertinent to consideration of the SGP 16/70 Project-specific adjustment factor. Environment Canada states:

> Without a sound basis for doing so (i.e. it cannot be a default assumption), **the human health risk assessor should not simply mathematically spread out a short-term dose over a long period and conclude that the short-term dose is toxicologically equivalent to a lower dose over the long period. In short, CSD recommends that the exposure be averaged over the total actual exposure period and compared with the appropriate TRV.** A scientific rationale is required to support any proposed amortization (dose averaging beyond actual exposure period) to ensure that short-term risks are not underestimated. This analysis needs to be done on a chemical-specific basis.[40] (emphasis added)

[38] Exhibit F. Environment Canada, *Interim Guidance on Human Health Risk Assessment for Short-Term Exposure to Carcinogens at Contaminated Sites* (2015).
[39] Exhibit F; Exhibit E.
[40] Exhibit F at 18.

82. TRV is the equivalent of the Idaho AACC. For the past 30 years Idaho has implemented the TAPs rule as Environment Canada recommends, providing a health-protective MOS that appropriately protects children, adolescents, and pregnancies. DEQ now proposes to endorse dose averaging through the three SGP Project-specific adjustment factors, increasing both cancer risk for these vulnerable populations and regulatory burden for PTC applicants.

83. Two examples of relevance to the SGP Project-specific adjustment factors demonstrate the inadequacy of the risk calculations offered by Paden and Lopez. A comprehensive HIA addressing arsenic at mining sites would address 1) Mode of Action (MOA); and 2) non-carcinogenic risk as these relate to critical life stages.

84. **MOA Considerations**: As the Lopez Declaration notes, arsenic is not considered a carcinogen exhibiting mutagenic MOA by the EPA at this time. Current EPA guidance does not specifically recommend applying the age-dependent adjustment factors to the arsenic inhalation URF. Current EPA policy requires life-stage adjustment for known mutagenic MOA carcinogens but leaves it to the risk assessment and risk managers' discretion whether to apply age-adjustments for carcinogens with unclear MOAs.[41] Some jurisdictions recommend applying age dependent adjustment factors to carcinogens for which the MOA is not definitive.[42] A comprehensive risk assessment would inform the risk management decision-makers that there is evidence suggesting arsenic, in combination with other co-stressors, has shown mutagenic

[41] Exhibit D.
[42] Exhibit G, California EPA, OEHHA, *Technical Support Document for Cancer Potency Factors: Methodologies for derivation, listing of available values, and adjustments to allow for early life stage exposures* (May 2009) at 3.

MOA.[43,44] A comprehensive risk assessment would inform the risk management decision-makers that there is evidence suggesting arsenic, in combination with other co-stressors, has shown mutagenic MOA.

85. **Non-carcinogenic Risk.** Environment Canada notes specific examples of non-carcinogenic arsenic health effects that can become the risk driver after applying age-specific exposure, absorption, and dose accumulation adjustments at contaminated sites where children may ingest, in addition to inhaling, arsenic laden dusts.[45]

86. Allocating a lifetime of allowable arsenic intake to children in 6 or 16 years, raises numerous non-carcinogenic concerns not mentioned in the Respondents' limited risk analyses.

87. The largest source of arsenic at the SGP are haul road fugitive dusts. Application of the SGP Project-specific adjustment factor allows the SGP to increase annual emission rates from haul roads by four to ten times more than that allowed under proper implementation of the TAPs rule.

88. This concentration of emissions in early childhood, not only increases ambient air arsenic concentrations, but more than quadruples the rate of arsenic laden dust deposition. It is well-known, in Idaho, nationally and internationally, that incidental ingestion of mining-related fugitive dusts is the major childhood exposure route for heavy metals in mining communities. Numerous DEQ risk assessments for abandoned mine sites in Idaho, including several at the

[43] Exhibit H, Environmental Health Perspectives, *Low-dose Arsenic: In Search of a Risk Threshold*, 122:5 (May 2014).
[44] Exhibit I. Speer, R.M., *et. al.*, *Arsenic and cancer: evidence and mechanisms*, Adv. Pharmacol. 96:151-202 (2023).
[45] Exhibit F at 18.

Bunker Hill and Coeur d'Alene Basin Superfund Site, have historically involved fugitive dusts from mining sites.[46, 47]

89. The EPA and DEQ Superfund regulators routinely apply age-dependent adjustment factors similar to those required for carcinogens that exhibit mutagenic MOAs.[48] There has been no consideration of non-carcinogenic risk for the SGP. Figures 3 and 5, above, demonstrate there is no need to assess other potential sources or non-carcinogenic risk if the TAPs rule is implemented properly using the **maximum one-year annual average carcinogen concentration**. Dust deposition would occur at rates anticipated under proper application of the TAPs rule. As a result, properly complying with the cancer risk criteria is also protective of non-carcinogenic risk.

90. The Paden and Lopez Declarations contain extremely limited risk calculations. Both Respondents use the inappropriately derived dose-averaged ambient concentration of 0.00095 $\mu g/m^3$ to calculate an alleged $4x10^{-6}$ cumulative cancer risk and assert compliance with EPA risk assessment policy. Both Respondents refer to the same EPA formulae found in Superfund guidance and simply compare the same long-term 70-year average value to the same range of alleged EPA allowable risk levels. Neither considers pertinent risk co-factors, vulnerable life stages, other potential sources, or a variety of other considerations inherent in the Idaho TAPs compliance strategy or MOS noted above. Neither mentions nor indicates understanding of the incremental nature of the TAPs Rule.

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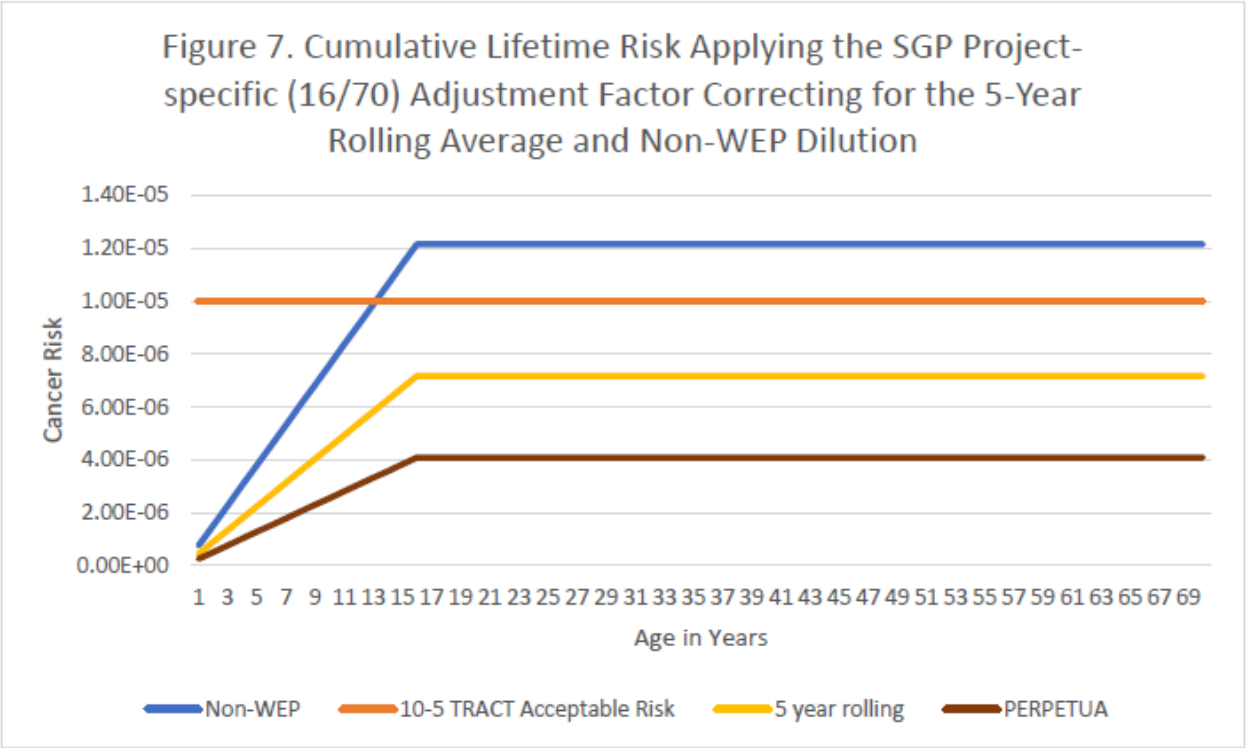
[46] Exhibit J. von Linder, I.H., *et. al.*, *Estimating Children's Soil/Dust Ingestion Rates through Retrospective Analyses of Blood Lead Biomonitoring from the Bunker Hill Superfund Site in Idaho*, Envtl. Health Perspectives, 124:9, 1462-1470 (2016).
[47] Exhibit K. U.S. EPA, *Estimation of Age-specific Soil and Dust Ingestion Rates for U.S. Children: Update to the Default Values for the Integrated Exposure Uptake Biokinetic Model for Lead in U.S. Children* (2021).
[48] Exhibit K.

91. Were the proper TAPs analysis conducted, the cumulative risk for long-term operations would be 5.1 $x10^{-5}$, as noted above. Figure 6, above, illustrated the sequential application of the three SGP Project-specific adjustment factors applied by DEQ (i.e., 5-year rolling average,, non-WEP sources, and 16/70 lifetime adjustment). The final 16/70 exposure dilution yields a cancer risk of $4.1x10^{-6}$. DEQ and the Respondents allege that 40% of the full lifetime allowable exposure is expended by the 16 years of SGP operations.

92. The $5.1x10^{-5}$ carcinogenic risk calculated for the SGP as TAPs requires does assume a 70-year basis. Figure 7 shows the application of the proper **maximum one-year annual average ambient air carcinogen concentration** (0.0125 $\mu g/m^3$) applied to the same 16-year LOM formulae used by the Respondents. After correcting for the 5-year rolling average and non-WEP adjustment factors disguised risk averaging steps, the cumulative risk after the16-year LOM is 1.2 x 10^{-5}.



93. This cumulative risk exceeds the allowable risk criteria by 20% using DEQ and Perpetua's calculation. Figure 7 also illustrates the effect of the serial application of SGP Project-specific 5-year rolling average and non-WEP Project-specific adjustment factors on cumulative cancer risk from the critical receptor viewpoint. Removing these dilution adjustments shows the individual receptor will experience a full lifetime allowable carcinogenic $1x10^{-5}$ equivalent exposure by year 13.

94. This opinion concludes that DEQs use of the ad hoc SGP Project-specific adjustment factors undermines the health protectiveness of the TAPs rule. The TAPs rule was specifically developed to avoid requiring risk assessment analyses by providing an inherent margin of safety (MOS). These SGP Project-specific adjustment factors facilitate cancer dose-averaging risk calculations that allow the SGP to significantly increase arsenic emissions

based on short-term Life of Mine (LOM) assumptions, but to nevertheless average the risk associated with those increased emission over 70-years.

95. This transfer of risk from the mine to the receptor's lifetime significantly reduces the MOS and negates the health protectiveness of the TAPs rule. The TAPs rule simply offers 10-fold increases in allowable risk, or emissions, for either 1) short-term projects of less than 5 years, or 2) T-RACT based relief based on available technology.

96. There is neither a provision, nor a need, for risk assessment if the TAPs Rules are properly implemented based on annual compliance with **maximum one-year annual average ambient air carcinogen concentration**. This application of the TAPs rule has served Idaho well for three decades. This policy change allowing risk averaging through the SGP Project-specific adjustment factors not only undermines the health protectiveness of the individual applicant source, but also the Statewide strategy that keeps all Idahoans safe with minimal regulatory burden.

DATED: October 4, 2024

Ian H. Von Lindern, P.E., Ph.D.

Exhibit A

Ian H. von Lindern, Ph.D., P.E.

Moscow, Idaho, USA
Ian@terrafound.org |+1 208 596 8577

Education

Ph.D., Environmental Science and Engineering, Yale University, 1980
M.F.S., Biometeorology and Atmospheric Studies, Yale University, 1973
B.S., Chemical Engineering, Carnegie-Mellon University, 1971

Professional & Technical Certifications

Professional Engineer, Idaho # 3044 ChE (1975)

Professional Experience

Ian von Lindern is co-founder of TerraGraphics International Foundation (TIFO), a non-profit humanitarian environmental response organization. He served as Chief Executive Officer and Principal Scientist of TerraGraphics Environmental Engineering Inc. from 1984-2014. Under his direction, TerraGraphics developed into a one-hundred person multidisciplinary environmental firm, specializing in the design and management of complex projects including site characterization, risk assessment, hazardous waste remediation, engineering design, GIS and database, and remediation oversight. He has 46 years of national and international engineering and scientific experience that includes a variety of environmental assessments; studies in air, water, and soil pollution; toxic and hazardous materials investigations; remedial and cleanup plans; human health risk assessments; and application of statistical analysis techniques to multidisciplinary environmental problems. He has directed more than 40 major health/environmental projects including primary and secondary smelters, used battery processors, landfills, uranium mill tailings, and organic chemical waste sites in the U.S. He has designed and implemented international health risk assessment/remediation projects in countries with high levels of childhood morbidity and mortality including Russia, China, Peru, Bangladesh, Dominican Republic, Senegal, Nigeria, and Kyrgyzstan.

As a Principal Scientist at TIFO, Dr. von Lindern works with marginalized mining and recycling communities around the world to address pollution-related health and environmental issues. Projects are implemented at the local level acknowledging diverse ethnic, religious, socio-economic, and geographic backgrounds to protect future generations and maintain livelihoods in vulnerable communities. TIFO's mission focuses on building environmental health capacity in both the host countries and the next generation of US scientists by sponsoring and directing collaborative projects, pairing US and local professionals and students; and encouraging programmatic research publications summarizing project outcomes and lessons learned. Since 2010, TIFO has partnered with Médecins Sans Frontières (MSF, Doctors Without Borders) in implementing joint medical, public health and environmental responses. TIFO's recent projects are evolving into a global juxtaposition of simultaneously assisting indigenous and disadvantaged communities in both the US and poor/middle income countries responding to the exponential demand for gold and green-energy technologies in the US, central Asia and west Africa. These projects offer promise of reviving a specialty metals industry in the US and providing subsistence incomes for poor populations suffering from climate-related loss of traditional agricultural and pastoral support systems. Conversely, there is the potential for catastrophic health and environmental damages. US efforts involve rigorous technical analysis of sophisticated regulatory environmental impact and permit applications, conveying that to uninformed communities, and advocating for the highest levels of environmental responsibility. Responses in poor countries involve identifying and implementing protective measures achievable within the socio-economic, political and economic capacity of the community. International projects often involve developing practicable community, family, and individual worker level health interventions, as governments often lack the resources and capacity to effectively regulate industry in either the artisanal or formal sectors.

Dr. von Lindern has served as an EPA Science Advisory Board and Clean Air Scientific Advisory Committee (CASAC) Subcommittee Member on several occasions, including: EPA Criteria Assessment Committee for Lead in the Ambient Air (1975-1977), and subsequent CASAC NAAQS lead reviews (1982-1986, 2006-2008); Review Subcommittee Assessing the Use of the Biokinetic Model for Lead Absorption in Children at RCRA/CERCLA Sites (1988); Subcommittee Assessing the Consistency of Lead Health Regulations in U.S. EPA Programs (1992); SAB Review Subcommittee for Urban Soil Lead Abatement Demonstration Project (1993); the Ad Hoc All-Ages Lead Model (AALM) Review (2005-2007, 2019-2020); External Peer Review of EPA's Draft Report – Proposed Modeling Approaches for a Health-Based Benchmark for Lead in Drinking Water (2017).

Project Experience
Example Consulting Projects Directed by Dr. von Lindern

Bunker Hill Mining and Metallurgical Complex/Coeur d'Alene Basin Superfund Site, Idaho, 1974–2016

Dr. von Lindern has worked for the State of Idaho on various projects involving the Bunker Hill/Coeur d'Alene Basin Superfund Site for more than 40 years, both as the lead Risk Assessor and as TerraGraphics Project Manager for the State of Idaho CERCLA activities. In 1974, as an Environmental Engineer for the State of Idaho, he directed the field study of lead intoxication in children surrounding the Bunker Hill smelter. As the state oversight contractor for more than 20 years, his duties have included initial contact with local leaders, assisting IDEQ in Cooperative Agreement and PRP negotiations, legislative committee presentations, moderating Task Force meetings, reviewing PRP and EPA activities, and developing the risk management strategy and site-specific cleanup criteria. He has a number of peer-reviewed publications on the reduction of childhood blood lead levels and remedial activities at this site. He also represented the IDEQ at the National Academy of Sciences (NAS) review of this Project in Washington D.C. (Superfund and Mining Megasites Lessons Learned from the Coeur d'Alene River Basin, (NRC 2005)).

Washington State Department of Justice – Natural Resources Division Litigation Support and Expert Witness, Northeastern Washington State, December 2009– December 2012

Dr. von Lindern provided expert witness testimony and reports for numerous enforcement and civil environmental liability lawsuits and litigation at sites throughout the United States. He was Principal-in-Charge for a contract with the Washington State Attorney General Office, Natural Resources Division, regarding potential mining contamination in northeastern Washington state. He and other TerraGraphics personnel researched and visited numerous abandoned mine sites and collected samples to assess metal contamination. Dr. von Lindern provided his expert opinion to the client for litigation support.

Trail of the Coeur d'Alenes and Bayhorse Ghost Town Remediation and Idaho State Parks and Recreation (IDPR) Development

The Bayhorse Mine property is a well-known "ghost town" near Challis, Idaho with substantial historic value. After completion of an ASTM Phase I ESA and All Appropriate Inquiry standards, the IDPR was considering the site for development as a State of Idaho Park and wanted to ensure the site was suitable for such use. Dr. von Lindern led the team that completed the assessment of human health risk and water quality concerns for the purchase of the Bayhorse Mine property. After the assessment, IDPR successfully acquired the Bayhorse Mine properties for converting the "ghost town" and associated abandoned mine holdings into a cultural, historical, and adventure recreation park.

The Park design mimics innovative risk management strategies used at the Trail of the Coeur d'Alenes State Park in northern Idaho. Dr. von Lindern assisted IDEQ, IDPR, the U.S. EPA and other related agencies at both Parks by developing a risk management strategy that is protective of human health and the

environment, while allowing public access and preserving the historic and recreational value of the resource. The Park opened to the public in June 2009.

Example TIFO Humanitarian / Non-Profit Projects Directed by Dr. von Lindern

In 2005, the US National Academy of Sciences' exhaustive review of the BHSS cleanup effort determined the health response methodologies were sound and effective. Subsequently, Dr. von Lindern co-led the joint Research & Development initiative between TerraGraphics and the University of Idaho to apply environmental cleanup methodologies developed in Idaho mining districts to hazardous waste sites in low and middle-income countries. Humanitarian cleanups were undertaken in conjunction with local governments, universities, and NGOs in a variety of cultural, socio-economic and governmental venues in Russia, China, Dominican Republic, Senegal, and Nigeria. In 2012, he and Dr. Margrit von Braun sold the for-profit firm and founded TIFO as an independent non-profit organization to assist international communities in remediating hazardous waste sites. TIFO has conducted workshops and human health risk assessments in Kyrgyz Republic, Armenia, Slovenia, Bangladesh, and Mongolia in collaboration with local governments, universities, hospitals, and NGOs, including the international humanitarian organization Médecins Sans Frontières (MSF, Doctors Without Borders).

Lead Poisoning – Emergency Health Response, Haina, Dominican Republic 2007-2011.

The community of Paraiso del Dios bordered a former used lead acid battery recovery operation in the port city of Haina near Santo Domingo. In 1997, several hundred children were surveyed and found to have a mean blood lead level of 71 μg/dL (range: 9-234 μg/dL); twenty-eight percent (28%) of children required immediate medical treatment. Residents reported that several children suffered seizures during the factory's operational years and continue to exhibit learning disabilities. The factory closed in 2000 and a repository for waste materials was developed on-site. The site was then abandoned and was subject to extensive uncontrolled salvage activities. The concrete retaining wall was scavenged, releasing large amounts of buried waste into the community during rain events. The exposed wastes, exceeding 30% lead, were sold as scrap. Highly contaminated materials were recycled and used as building material and fill in the adjacent community. Children from the surrounding community accessed the industrial site on a daily basis, tracking soils from the site and exposing the rest of their families.

Dr. von Lindern designed and directed a sampling and risk assessment program in 2006-07, when the area was named one of the world's top ten most polluted sites. Extremely high lead concentrations were found on site and in adjacent residential lots. Contaminated wastes in the failed repository showed concentrations from 30% to 45% lead. Surface soil lead concentrations ranged from 4,000 to >300,000 mg/kg, orders of magnitude above the USEPA limit of 400 mg/kg. The project team then collaborated with the Ministries of Health and Environment to develop an intervention strategy recommending a blood lead monitoring and follow-up program, relocation of all high-level wastes to an off-site repository, an on-site repository for the low-level and mid-level soils, and dedication of the property as a public park with appropriate institutional controls to ensure sustainability. A blood lead monitoring program began in 2007 and found 80% of children >10 μg/dL, 24% >40 μg/dL, and 7% >70 μg/dL. In 2008, the Dominican Republic government commissioned a cleanup in which Dr. von Lindern provided technical assistance. More than 3000 cubic meters of hazardous wastes and 4000 cubic meters of contaminated soils were removed. The site was turned in to an "ecological park" with a dedication ceremony in 2010. The Ministry of Environment introduced the park as the first step in initiating a cleanup program for the entire country and dedicated an "ecological mural" to the Dominican environment and "heroes" of the cleanup effort.

Lead Poisoning – Emergency Health Response, Dakar, Senegal 2009-2011.

Thiaroye Sur Mer (TSM) was the site of Used Lead Acid Battery recovery since the 1970s. Multiple groups recovered lead from batteries to manufacture weights for local fishermen. Several thousand tons of discarded

battery sludge accumulated in the area over three decades. In 2007, dramatic increases in lead prices stimulated East Indian traders to purchase the lead oxide sludge. To minimize shipping costs, 200 local women were employed to sift out beach sand that had accumulated with the sludge. The process involved transporting, drying, sifting, and bagging the lead dust. Bags of lead product were stored in homes prior to sale. Many mothers brought their infants and toddlers with them to work. In 2007-08, 18 children died as a direct result of lead exposures. Mean blood lead levels in children were >100 μg/dL and individual levels were >350 μg/dL

Limited emergency remediation activities were undertaken in April and May of 2008. Three-hundred (300) tons of lead were removed from local homes. The World Health Organization (WHO) tested siblings of the deceased children and forty-one children were subsequently hospitalized and placed in temporary foster care. Massive flooding of the area during the rainy season delayed further action. After the flood subsided, TIFO collaborated with other partners to conduct extensive sampling and interviews of the TSM population. In collaboration with the Ministries of Health and Environment, Dr. von Lindern developed a health response and remediation strategy that was implemented in April 2009. The strategy included establishment of sentinel homes in the community where intensive interviews and sampling were conducted to determine the extent and severity of continuing exposures and to identify active lead exposure pathways. These homes and resident children were monitored to assess the effectiveness of the cleanup.

Lead Poisoning – Emergency Health Response, Zamfara and Niger State, Northern Nigeria, May 2010–Present

Beginning in 2010, Dr. von Lindern spent several months in northern Nigeria directing the characterization and remediation of the world's worst lead poisoning epidemic. The 2010-2013 epidemic in Zamfara, Nigeria was unprecedented in morbidity, mortality, and in the environmental health response. More than 400 young children died from acute lead poisoning associated with artisanal gold mining. Soil removal protocols developed at the U.S. Bunker Hill Superfund Site were adapted to local resources, labor practices, and cultural traditions. Dr. von Lindern and other TerraGraphics personnel worked cooperatively with local authorities, MSF, the Centers for Disease Control (CDC), the World Health Organization, the Blacksmith Institute, and government officials and villagers in remote areas to develop an emergency response and remove contaminated soils.

In 2011, TerraGraphics was recognized by the United Nations Environment Programme (UNEP) and Green Cross International with the Green Star Award, given to every two years in association with UN reviews of its environmental programs to recognize those who have made remarkable efforts to prevent, prepare for, and respond to environmental emergencies around the world. In 2012-13, remediation progressed from emergency response by international personnel to comprehensive cleanup implemented by the Nigerian government. TerraGraphics humanitarian successor, TIFO, partnered with MSF to provide guidance and assistance the Nigerian Federal, Zamfara State and local governments in the completion of the largest and most comprehensive cleanup implemented and funded by an African government. More than 27,000 m^3 of contaminated soils were removed from 820 residential areas and ore processing areas in eight villages, largely by hand labor, and disposed of in constructed landfills. Soil lead exposures decreased 97% for more than 17,000 villagers, allowing chelation treatment of 2349 children. Mean blood lead levels for children ≤5 years age declined from 173 μg/dL to <20 μg/dL over the four-year US $5M remedial program.

Subsequently, TIFO, MSF and other NGOs assisted local, state, and federal leadership in implementing long-term prevention and management programs in Zamfara State. In 2016, a second ASGM poisoning event killed 28 children in neighboring Niger State. The federal government requested TIFO assistance and mobilized trained technicians from Zamfara to lead the assessment and cleanup. Remediation was fully implemented with Nigerian funds, and Niger State assumed takeover of both medical and environmental operations and maintenance in 2018. This successful application was the impetus for the Nigerian Ministry of Mines and Steel/World Bank/MSF/TIFO sponsored Conference in Abuja in 2018, examining the legalization and support of ASGM as a mechanism to address poverty and population displacement in the Sahel, employing safer-mining initiatives.

Continued TIFO-Médecins Sans Frontières Collaborations: Bangladesh and Kyrgyzstan 2011-Present.

In 2014, following successful collaborations in west Africa, MSF and TIFO's partnered to assess and address pollutant-related hazards at formal and informal leather tanneries; small-scale plastic, aluminum, foundry, and textiles recycling operations; and artisanal family-scale scavenging and waste recovery and reuse operations in urban slums in Dhaka, Bangladesh. MSF has since been operating occupational health clinics employing environmental health/occupational remedies for several thousand workers and families.

Since 2016, TIFO and MSF have partnered with the Kyrgyz Ministry of Health (MOH) assessing the potential, and emergency response considerations, for seismic and climate-related catastrophic release of legacy mining and smelting hazardous wastes accumulated over 70 years of operations at the former Soviet Union's largest mercury and antimony factories. TIFO provided assistance with Staff Health and Safety planning and performing a Human Health Risk Assessment for women and children's health issues in the mercury/antimony/gold mining communities. In 2019, the joint TIFO/MSF/MOH team collected >500 soil, air, water and food samples to support health assessment and target blood, urine and hair surveys scheduled for summer 2020. These results will support establishing environmental/occupational health monitoring/intervention capacity in the local government, as Kyrgyz officials revitalize the Soviet-era mining operation to support the local economy and meet the growing demand for mercury in ASGM.

Gold and Strategic Minerals Development Impact Evaluations on Historic Tribal Lands, Intermountain West, USA, 2020 – Present.

TIFO's mission is to assist mining and mineral processing communities to operate as safely as practicable while maintaining essential economic activities. The unprecedented demand for gold and strategic metals has prompted several major exploration and mineral development proposals in western states. TIFO's international mission includes assessing and responding to health and environmental impacts of polluting activities on sovereign native and tribal lands within the US. In that regard TIFO supports scientifically-sound and transparent analyses of the environmental and human health issues faced by mining communities, and the development of solutions implemented within local socio-economic and cultural capabilities. Proposed gold, antimony, and cobalt mining in Idaho, Nevada and Washington States have the potential to adversely affect several reservations and aboriginal tribal lands. The Idaho Stibnite Gold Mine proposal, that claims it will meet 33% of the US antimony demand, is of interest because both the industry and the US regulatory arena have the capacity to implement best practices that are not available to poor communities throughout the world. Mining advocates allege these developments will be safe and secure, and are projecting unprecedented control levels for toxic contaminants. Conversely, the mining company consultants are arguing for relief from environmental regulatory requirements in these mining-friendly states. However, citizen-based interest groups and tribal authorities have limited capacity and resources to evaluate the complex environmental assessments and permit applications. Ironically, the Stibnite Gold Project is exploiting the same ores and metallurgical processes as the gold/antimony mining TIFO is assessing in Kyrgyzstan. As there are currently no smelters in the US that can process the antimony concentrates, the Idaho ores are currently projected to be exported to the same Chinese smelters processing the Kyrgyz ores. Through TIFO, Dr. von Lindern is providing independent review of these documents and submitting comments to the review agencies.

Regulatory Knowledge

Ian von Lindern has worked on projects regulated under Federal, State, local, and foreign regulations, including CERCLA, TSCA, CWA, CAA, NESHAPs, DOT, EPRCRA, SARA, NEPA, and RCRA in the U.S. He has provided litigation support and expert witness testimony in administrative and court proceedings. He has served on several U.S. government advisory panels, including the appointments pertinent to lead health and remediation as shown in the list below.

Ian H. von Lindern, Ph.D., P.E.

Special Appointments/Memberships/Affiliations

U.S. EPA Science Advisory Board. Peer Review. All Ages Lead Model (AALM). Washington, DC. October 16-20, 2019.

U.S. EPA External Peer Review. Draft Report, Proposed Modeling Approaches for a Health Based Benchmark for Lead in Drinking Water. Prepared for: U.S. Environmental Protection Agency, Office of Water, Washington, DC. June 27-28, 2017.

U.S. EPA External Peer Review. EPA's Approach for Estimating Exposures and Incremental Health Effects from Lead due to Renovation, Repair, and Painting Activities in Public and Commercial Buildings. Prepared for: U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC. January 2015.

U.S. EPA Science Advisory Board (CASAC). Review of the Integrated Science Assessment (ISA) for Lead in the Ambient Air. US EPA, Washington, D.C. 2012-2013

American University of Armenia, School of Public Health, Yerevan. Invited Professor, Graduate course Risk Assessment for Environmental Health Professionals for Master of Public Health (MPH) Students. 2012-present.

U.S. Centers for Disease Control and the Harvard University School of Public Health Initiative to address health effects of mining and smelting in the developing world. 2009-2013.

Affiliate Professor of Chemical Engineering, University of Idaho, Moscow, Idaho, 1981–2011

U.S. EPA Science Advisory Board. Review of the Lead National Ambient Air Quality Standard for Lead. U.S. EPA, Washington, DC. 2006-2008.

U.S. Clean Air Scientific Advisory Committee (CASAC). Review of the Air Quality Criteria Document for Lead. U.S. EPA, Washington, DC. 2010-2013, 2006-2007.

U.S. EPA Science Advisory Board. Review of EPA's Lead Renovation, Repair and Painting (LRRP) Activities. U.S. EPA, Washington, DC. 2007.

U.S. EPA Science Advisory Board. Review of EPA's Ad Hoc All-Ages Lead Model (AALM) Review Panel. U.S. EPA, Washington, DC. 2007.

U.S. EPA Science Advisory Board. Review Subcommittee for Urban Soil Lead Abatement Demonstration Project. U.S. EPA, Washington, DC, 1993-1995.

NIEHS Select Reviewer Grants Review Committee, Superfund/Hazardous Workers Training Program, NIEHS, RTP, NC. 1992.

Advisory Committee for Development of Lead Paint Abatement Guidelines for Public Housing in the United States, U.S. Dept of HUD, Washington, D.C., 1992.

U.S. EPA Science Advisory Board, Subcommittee Assessing the Consistency of Lead Health Regulations in U.S. EPA Programs, Special Report to the Administrator, Washington, D.C., 1992.

U.S. EPA Science Advisory Board, Review Subcommittee Assessing the Use of the Biokinetic Model for Lead Absorption in Children at RCRA/CERCLA sites. U.S. EPA, Washington DC, 1991.

Technical advisor and consultant to Latah County and North Central Health District Regional Solid Waste Advisory Committees, Moscow and Lewiston, ID. 1991.

Technical advisor to the National Alliance to End Lead Poisoning in Children, Washington, D.C. 1991-2001

NIEHS Select Reviewer Grants Review Committee, Superfund/Hazardous Workers Training Program, NIEHS, Research Triangle Park, NC, 1989-1993.

U.S. EPA Clean Air Scientific Advisory Committee (CASAC) Member, Subcommittee on Exposure Assessment Methodology, U.S. EPA, Washington D.C. 1988.

U.S. EPA Criteria Assessment Committee for Lead in the Ambient Air, RTP, NC. 1975-1986.

Additional Certifications/Training

PSMJ Conference for CEOs-2005

Ian H. von Lindern, Ph.D., P.E.

Publications

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von Braun, MC, von Lindern, IH, Martyn, S, Steward K. Use of a Geographic Information System in Selecting Residential Properties for Remediation at the Bunker Hill National Priorities List Site. Proceedings of the 10th National Conference on Management of Uncontrolled Hazardous Waste Sites, Superfund, Washington, D.C. November 1989.

von Lindern, I, von Braun, MC. Reconstructive Analysis of Lead Exposures in a Smelter Community Using Geographic Information System Techniques. Proceedings of Society for Occupational and Environmental Health Conference, Washington D.C. April 1988.

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Reports/Presentations

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Data Summary Report: Summary of Results from Field and Laboratory Activities from August-September 2019 Environmental Assessment in Aidarken and Chauvay, Kadamjay Rayon, Kyrgyz Republic. Prepared for Kyrgyz Ministry of Health and Médecins Sans Frontières. 13 November 2020.

Mining, Climate Change, and Conflict: Lessons from Nigeria and Kyrgyzstan. Society for Mining, Metallurgy, and Exploration, Southern California Chapter (virtual). 12 November 2020.

Local and regional impacts of primary mercury production on environmental health and security in Batken, Kyrgyzstan. Ramazzini Days Conference. Carpi, Italy (virtual). 24 October 2020.

Review of Existing Information and Identification of Data Gaps for Conducting Human Health Risk Assessments (HHRA) and Biomonitoring for Heavy Metal Exposures – Khaidarken, Batken Province, Kyrgyz Republic. Prepared for Kyrgyz Ministry of Health and Médecins Sans Frontières. April 2019.

Presenter: Achievement Awardee Luncheon Presentation – International disparities in childhood lead poisoning: following metal production to the world's most vulnerable communities. Association for Environmental Health and Sciences Foundation. 29th Annual Conference on Water, Soils, Sediments, and Air. San Diego, CA, USA. 18-22 March 2019.

Eight Years, Two States, Ten Villages, and Five Thousand Children: Adapting US Superfund Methodologies to Lead Remediation in Northern Nigeria. Association for Environmental Health and Sciences Foundation. 29th Annual Conference on Water, Soils, Sediments, and Air. San Diego, CA, USA. 18-22 March 2019.

Presenter: Environmental Health and Risk Assessment: Workshop on MSF and Extractive Industries. Médecins sans Frontières, Geneva, Switzerland. 24-25 October 2018.

Instructor, Assessment and Remediation of Heavy Metal Contamination, Workshop on Extractive Industries, Médecins sans Frontières, Geneva, Switzerland, October 2018.

Presenter: Humanitarian Crisis in Pollution-Related Disease: MSF's role, response models, and discussions on the path forward. Workshop for Médecins Sans Frontières. Geneva, Switzerland. 16-17 April 2018.

Final Seismic Risk Addendum Report: Exposure Risks Related to Seismic Hazards and Risks in Batken, Kyrgyzstan. Prepared for Médecins sans Frontières. March 2019.

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Escalating community metals poisoning due to changes in the global economy. Living in a Chemical World Session III, Proceedings of Ramazzini Days Conference. Carpi, Italy. October 2015.

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Artisanal Mining Lead Poisoning Epidemic, Zamfara State, Nigeria, 2010-11, Phase I and II Emergency Response Cleanup. Prepared for: Médecins Sans Frontières. Prepared by: TerraGraphics Environmental Engineering. October 2011.

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The Life Cycle of Metals: Improving Health, Environment and Human Security, Symposium. University of Tokyo and Harvard University. Tokyo, Japan. October 2011.

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Health Response to the World's Worst Lead Poisoning Epidemic, Zamfara, Nigeria 2010-11 Presentation to U.S. Environmental Protection Agency Headquarters, International Programs. July 2011.

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Lead Poisoning -The World's Worst are Becoming Worse. More Children at More Places are More Severely Poisoned. Presentation to the U.S. Centers for Disease Control, Lead Poisoning Program. Atlanta, Georgia. April 2011.

A Comprehensive Approach to Remediation of the Lead Poisoning Epidemic in Zamfara. Presentation to the Nigerian Public Health Association, Annual Conference. Abuja, Nigeria. March 2011.

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Exhibit B

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Environmental Protection
Agency

Office of Health and
Environmental Assessment
Washington DC 20460

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Research and Development

EPA

The Risk Assessment Guidelines of 1986

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August 1987

THE RISK ASSESSMENT GUIDELINES OF 1986

U.S. Environmental Protection Agency
Washington, D.C.

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CONTENTS

PREFACE

On September 24, 1986, the U.S. Environmental Protection Agency (EPA) issued risk assessment guidelines relating to five areas: carcinogenicity, mutagenicity, chemical mixtures, suspect developmental toxicants, and estimating exposures (51 FR 33992-34054). The guidelines were developed to promote high technical quality and Agencywide consistency in the risk assessment process.

The guidelines were developed partly in response to a 1983 National Academy of Sciences publication entitled "Risk Assessment in the Federal Government: Managing the Process," which recommended that Federal regulatory agencies establish risk assessment guidelines. An EPA task force, convened by then Administrator William D. Ruckelshaus to study ways to improve the scientific foundation for Agency regulatory decisions, accepted the recommendation, and work on the guidelines began early in 1984.

The guidelines are products of a two-year Agency development and review process which included many scientists from the larger scientific community. They were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment in the Agency's Office of Research and Development. The scientists involved were skilled in each topic, and early drafts were peer-reviewed by experts from academia, industry, public interest groups, and other governmental agencies. Subsequently, proposed guidelines were published in the *Federal Register*, reviewed by special panels of EPA's Science Advisory Board (SAB), and revised to take into account public and SAB comments. After final EPA review and Office of Management and Budget review, the guidelines were signed by EPA Administrator Lee M. Thomas on August 22, 1986, and published in the *Federal Register* on September 24, 1986.

Each of the five guidelines provides both technical information and science policy guidance relating to the conduct of EPA risk assessments and presentation of risk assessment information. The guidelines are sufficiently flexible to allow skilled scientists to make appropriate technical judgments on a case-by-case basis, giving full consideration to all relevant scientific information. The guidelines also stress that risk assessments should include a discussion of the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment. They require risk assessors to inform Agency decisionmakers and the public about the assumptions used in and the implications of individual risk assessment conclusions, so that appropriate risk management decisions can be made and explained.

While these guidelines are published Agency documents, they should not be interpreted as static, but as the first step in the continuing process of identifying the best methods for assessing risk to environmental pollutants. Consequently, the risk assessment guidelines are constantly undergoing Agency scrutiny and will be revised in line with new methods and information, as appropriate.

This document presents the five guidelines as they originally appeared in the *Federal Register* but in a format that is easier to read.

ABSTRACT

On September 24, 1986, the U.S. Environmental Protection Agency issued risk assessment guidelines relating to five areas: carcinogenicity, mutagenicity, chemical mixtures, suspect developmental toxicants, and estimating exposures (51 FR 33992-34054). The guidelines were developed to promote high technical quality and Agencywide consistency in the risk assessment process. This document presents the five guidelines as they originally appeared in the *Federal Register* but in a format that is easier to read.

51 FR 33992

GUIDELINES FOR CARCINOGEN RISK ASSESSMENT

SUMMARY:On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for Carcinogen Risk Assessment.

The Guidelines for Carcinogen Risk Assessment (hereafter "Guidelines") are intended to guide Agency evaluation of suspect carcinogens in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for Carcinogen Risk Assessment published November 23, 1984 (49 FR 46294).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

FOR FURTHER INFORMATION CONTACT:

Dr. Robert E. McGaughy
Carcinogen Assessment Group
Office of Health and Environmental Assessment (RD-689)
401 M Street, S.W.
Washington, DC 20460
202-382-5898

SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process*. In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for Carcinogen Risk Assessment

Work on the Guidelines for Carcinogen Risk Assessment began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the field of carcinogenesis from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (49 FR 46294). On November 9, 1984, the Administrator directed that Agency offices use the proposed guidelines in performing risk assessments until final guidelines become available.

After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and proposed changes in the language of the guidelines to deal with the issues raised. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for Carcinogen Risk Assessment were concurred on in a letter dated February 7, 1986. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The Agency is continuing to study the risk assessment issues raised in the guidelines and will revise these Guidelines in line with new information as appropriate.

References, supporting documents, and comments received on the proposed guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will

[51 FR 33993]

have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

CONTENTS

Part A: Guidelines for Carcinogen Risk Assessment

I. Introduction

This is the first revision of the 1976 Interim Procedures and Guidelines for Health Risk Assessments of Suspected Carcinogens (U.S. EPA, 1976; Albert et al., 1977). The impetus for this revision is the need to incorporate into these Guidelines the concepts and approaches to carcinogen risk assessment that have been developed during the last ten years. The purpose of these Guidelines is to promote quality and consistency of carcinogen risk assessments within the EPA and to inform those outside the EPA about its approach to carcinogen risk assessment. These Guidelines emphasize the broad but essential aspects of risk assessment that are needed by experts in the various disciplines required (e.g., toxicology, pathology, pharmacology, and statistics) for carcinogen risk assessment. Guidance is given in general terms since the science of carcinogenesis is in a state of rapid advancement, and overly specific approaches may rapidly become obsolete.

These Guidelines describe the general framework to be followed in developing an analysis of carcinogenic risk and some salient principles to be used in evaluating the quality of data and in formulating judgments concerning the nature and magnitude of the cancer hazard from suspect carcinogens. It is the intent of these Guidelines to permit sufficient flexibility to accommodate new knowledge and new assessment methods as they emerge. It is also recognized that there is a need for new methodology that has not been addressed in this document in a number of areas, e.g., the characterization of uncertainty. As this knowledge and assessment methodology are developed, these Guidelines will be revised whenever appropriate.

A summary of the current state of knowledge in the field of carcinogenesis and a statement of broad scientific principles of carcinogen risk assessment, which was developed by the Office of Science and Technology Policy (OSTP, 1985), forms an important basis for these Guidelines; the format of these Guidelines is similar to that proposed by the National Research Council (NRC) of the National Academy of Sciences in a book entitled *Risk Assessment in the Federal Government: Managing the Process* (NRC, 1983).

These Guidelines are to be used within the policy framework already provided by applicable EPA statutes and do not alter such policies. These Guidelines provide general directions for analyzing and organizing available data. They do not imply that one kind of data or another is prerequisite for regulatory action to control, prohibit, or allow the use of a carcinogen.

Regulatory decision making involves two components: risk assessment and risk management. Risk assessment defines the adverse health consequences of exposure to toxic agents. The risk assessments will be carried out independently from considerations of the consequences of regulatory action. Risk management combines the risk assessment with the directives of regulatory legislation, together with socioeconomic, technical, political, and other considerations, to reach a decision as to whether or how much to control future exposure to the suspected toxic agents.

Risk assessment includes one or more of the following components: hazard identification, dose-response assessment, exposure assessment, and risk characterization (NRC, 1983).

Hazard identification is a qualitative risk assessment, dealing with the process of determining whether exposure to an agent has the potential to increase the incidence of cancer. For purposes of these Guidelines, both malignant and benign tumors are used in the evaluation of the carcinogenic hazard. The hazard identification component qualitatively answers the question of how likely an agent is to be a human carcinogen.

Traditionally, quantitative risk assessment has been used as an inclusive term to describe all or parts of dose-response assessment, exposure assessment, and risk characterization. Quantitative risk assessment can be a useful general term in some circumstances, but the more explicit terminology developed by the NRC (1983) is usually preferred. The dose-response assessment defines the relationship between the dose of an agent and the probability of induction of a carcinogenic effect. This component usually entails an extrapolation from the generally high doses administered to experimental animals or exposures noted in epidemiologic studies to the exposure levels expected from human contact with the agent in the environment; it also includes considerations of the validity of these extrapolations.

The exposure assessment identifies populations exposed to the agent, describes their composition and size, and presents the types, magnitudes, frequencies, and durations of exposure to the agent.

[51 FR 33994]

In risk characterization, the results of the exposure assessment and the dose-response assessment are combined to estimate quantitatively the carcinogenic risk. As part of risk characterization, a summary of the strengths and weaknesses in the hazard identification, dose-response assessment, exposure assessment, and the public health risk estimates are presented. Major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties embodied in the assessment are also presented, distinguishing clearly between fact, assumption, and science policy.

The National Research Council (NRC, 1983) pointed out that there are many questions encountered in the risk assessment process that are unanswerable given current scientific knowledge. To bridge the uncertainty that exists in these areas where there is no scientific consensus, inferences must be made to ensure that progress continues in the assessment process. The OSTP (1985) reaffirmed this position, and generally left to the regulatory agencies the job of articulating these inferences. Accordingly, the Guidelines incorporate judgmental positions (science policies) based on evaluation of the presently available information and on the regulatory mission of the Agency. The Guidelines are consistent with the principles developed by the OSTP (1985), although in many instances are necessarily more specific.

II. Hazard Identification

A. Overview

The qualitative assessment or hazard identification part of risk assessment contains a review of the relevant biological and chemical information bearing on whether or not an agent may pose a carcinogenic hazard. Since chemical agents seldom occur in a pure state and are often transformed in the body, the review should include available information on contaminants, degradation products, and metabolites.

Studies are evaluated according to sound biological and statistical considerations and procedures. These have been described in several publications (Interagency Regulatory Liaison Group, 1979; OSTP, 1985; Peto et al., 1980; Mantel, 1980; Mantel and Haenszel, 1959; Interdisciplinary Panel on Carcinogenicity, 1984; National Center for Toxicological Research, 1981; National Toxicology Program, 1984; U.S. EPA, 1983a, 1983b, 1983c; Haseman, 1984). Results and conclusions concerning the agent, derived from different types of information, whether indicating positive or negative responses, are melded together into a weight-of-evidence determination. The strength of the evidence supporting a potential human carcinogenicity judgment is developed in a weight-of-evidence stratification scheme.

B. Elements of Hazard Identification

Hazard identification should include a review of the following information to the extent that it is available.

1. *Physical-Chemical Properties and Routes and Patterns of Exposure.* Parameters relevant to carcinogenesis, including physical state, physical-chemical properties, and exposure pathways in the environment should be described where possible.

2. *Structure-Activity Relationships.* This section should summarize relevant structure-activity correlations that support or argue against the prediction of potential carcinogenicity.

3. Meta*bolic and Pharmacokinetic Properties.* This section should summarize relevant metabolic information. Information such as whether the agent is direct-acting or requires conversion to a reactive carcinogenic (e.g., an electrophilic) species, metabolic pathways for such conversions, macromolecular interactions, and fate (e.g., transport, storage, and excretion), as well as species differences, should be discussed and critically evaluated. Pharmacokinetic properties determine the biologically effective dose and may be relevant to hazard identification and other components of risk assessment.

4. To*xicologic Effects.* Toxicologic effects other than carcinogenicity (e.g., suppression of the immune system, endocrine disturbances, organ damage) that are relevant to the evaluation of carcinogenicity should be summarized. Interactions with other chemicals or agents and with lifestyle factors should be discussed. Prechronic and chronic toxicity evaluations, as well as other test results, may yield information on target organ effects, pathophysiological reactions, and preneoplastic lesions that bear on the evaluation of carcinogenicity. Dose-response and time-to-response analyses of these reactions may also be helpful.

5. *Short-Term Tests.* Tests for point mutations, numerical and structural chromosome aberrations, DNA damage/repair, and *in vitro* transformation provide supportive evidence of carcinogenicity and may give information on potential carcinogenic mechanisms. A range of tests from each of the above end points helps to characterize an agent's response spectrum.

Short-term *in vivo* and *in vitro* tests that can give indication of initiation and promotion activity may also provide supportive evidence for carcinogenicity. Lack of positive results in short-term tests for genetic toxicity does not provide a basis for discounting positive results in long-term animal studies.

6. *Long-Term Animal Studies.* Criteria for the technical adequacy of animal carcinogenicity studies have been published (e.g., U.S. Food and Drug Administration, 1982; Interagency Regulatory Liaison Group, 1979; National Toxicology Program, 1984; OSTP, 1985; U.S. EPA, 1983a, 1983b, 1983c; Feron et al., 1980; Mantel, 1980) and should be used to judge the acceptability of individual studies. Transplacental and multigenerational carcinogenesis studies, in addition to more conventional long-term animal studies, can yield useful information about the carcinogenicity of agents.

It is recognized that chemicals that induce benign tumors frequently also induce malignant

tumors, and that benign tumors often progress to malignant tumors (Interdisciplinary Panel on Carcinogenicity, 1984). The incidence of benign and malignant tumors will be combined when scientifically defensible (OSTP, 1985; Principle 8). For example, the Agency will, in general, consider the combination of benign and malignant tumors to be scientifically defensible unless the benign tumors are not considered to have the potential to progress to the associated malignancies of the same histogenic origin. If an increased incidence of benign tumors is observed in the absence of malignant tumors, in most cases the evidence will be considered as limited evidence of carcinogenicity.

The weight of evidence that an agent is potentially carcinogenic for humans increases (1) with the increase in number of tissue sites affected by the agent; (2) with the increase in number of animal species, strains, sexes, and number of experiments and doses showing a carcinogenic response; (3) with the occurrence of clear-cut dose-response relationships as well as a high level of statistical significance of the increased tumor incidence in treated compared to control groups; (4) when there is a dose-related shortening of the time-to-tumor occurrence or time to death with tumor; and (5) when there is a dose-related increase in the proportion of tumors that are malignant.

Long-term animal studies at or near the maximum tolerated dose level (MTD) are used to ensure an adequate power for the detection of carcinogenic

[51 FR 33995]

activity (NTP, 1984; IARC, 1982). Negative long-term animal studies at exposure levels above the MTD may not be acceptable if animal survival is so impaired that the sensitivity of the study is significantly reduced below that of a conventional chronic animal study at the MTD. The OSTP (1985; Principle 4) has stated that,

> The carcinogenic effects of agents may be influenced by non-physiological responses (such as extensive organ damage, radical disruption of hormonal function, saturation of metabolic pathways, formation of stones in the urinary tract, saturation of DNA repair with a functional loss of the system) induced in the model systems. Testing regimes inducing these responses should be evaluated for their relevance to the human response to an agent and evidence from such a study, whether positive or negative, must be carefully reviewed.

Positive studies at levels above the MTD should be carefully reviewed to ensure that the responses are not due to factors which do not operate at exposure levels below the MTD. Evidence indicating that high exposures alter tumor responses by indirect mechanisms that may be unrelated to effects at lower exposures should be dealt with on an individual basis. As noted by the OSTP (1985), "Normal metabolic activation of carcinogens may possibly also be altered and carcinogenic potential reduced as a consequence [of high-dose testing]."

Carcinogenic responses under conditions of the experiment should be reviewed carefully as they relate to the relevance of the evidence to human carcinogenic risks (e.g., the occurrence of bladder tumors in the presence of bladder stones and implantation site sarcomas). Interpretation of animal studies is aided by the review of target organ toxicity and other effects (e.g., changes in the immune and endocrine systems) that may be noted in prechronic or other toxicological studies. Time and dose-related changes in the incidence of preneoplastic lesions may also be helpful in interpreting animal studies.

Agents that are positive in long-term animal experiments and also show evidence of promoting or cocarcinogenic activity in specialized tests should be considered as complete carcinogens unless there is evidence to the contrary because it is, at present, difficult to determine whether an agent is only a promoting or cocarcinogenic agent. Agents that show positive results in special tests for initiation, promotion, or cocarcinogenicity and no indication of tumor response in well-conducted and well-designed long-term animal studies should be dealt with on an individual basis.

To evaluate carcinogenicity, the primary comparison is tumor response in dosed animals as compared with that in contemporary matched control animals. Historical control data are often valuable, however, and could be used along with concurrent control data in the evaluation of carcinogenic responses (Haseman et al., 1984). For the evaluation of rare tumors, even small tumor responses may be significant compared to historical data. The review of tumor data at sites with high spontaneous background requires special consideration (OSTP, 1985; Principle 9). For instance, a response that is significant with respect to the experimental control group may become questionable if the historical control data indicate that the experimental control group had an unusually low background incidence (NTP, 1984).

For a number of reasons, there are widely diverging scientific views (OSTP, 1985; Ward et al., 1979a, b; Tomatis, 1977; Nutrition Foundation, 1983) about the validity of mouse liver tumors as an indication of potential carcinogenicity in humans when such tumors occur in strains with high spontaneous background incidence and when they constitute the only tumor response to an agent. These Guidelines take the position that when the only tumor response is in the mouse liver and when other conditions for a classification of "sufficient" evidence in animal studies are met (e.g., replicate studies, malignancy; see section IV), the data should be considered as "sufficient" evidence of carcinogenicity. It is understood that this classification could be changed on a case-by-case basis to "limited," if warranted, when factors such as the following, are observed: an increased incidence

of tumors only in the highest dose group and/or only at the end of the study; no substantial dose-related increase in the proportion of tumors that are malignant; the occurrence of tumors that are predominantly benign; no dose-related shortening of the time to the appearance of tumors; negative or inconclusive results from a spectrum of short-term tests for mutagenic activity; the occurrence of excess tumors only in a single sex.

Data from all long-term animal studies are to be considered in the evaluation of carcinogenicity. A positive carcinogenic response in one species/strain/sex is not generally negated by negative results in other species/strain/sex. Replicate negative studies that are essentially identical in all other respects to a positive study may indicate that the positive results are spurious.

Evidence for carcinogenic action should be based on the observation of statistically significant tumor responses in specific organs or tissues. Appropriate statistical analysis should be performed on data from long-term studies to help determine whether the effects are treatment-related or possibly due to chance. These should at least include a statistical test for trend, including appropriate correction for differences in survival. The weight to be given to the level of statistical significance (the p-value) and to other available pieces of information is a matter of overall scientific judgment. A statistically significant excess of tumors of all types in the aggregate, in the absence of a statistically significant increase of any individual tumor type, should be regarded as minimal evidence of carcinogenic action unless there are persuasive reasons to the contrary.

7. Human Studies. Epidemiologic studies provide unique information about the response of humans who have been exposed to suspect carcinogens. Descriptive epidemiologic studies are useful in generating hypotheses and providing supporting data, but can rarely be used to make a causal inference. Analytical epidemiologic studies of the case-control or cohort variety, on the other hand, are especially useful in assessing risks to exposed humans.

Criteria for the adequacy of epidemiologic studies are well recognized. They include factors such as the proper selection and characterization of exposed and control groups, the adequacy of duration and quality of follow-up, the proper identification and characterization of confounding factors and bias, the appropriate consideration of latency effects, the valid ascertainment of the causes of morbidity and death, and the ability to detect specific effects. Where it can be calculated, the statistical power to detect an appropriate outcome should be included in the assessment.

The strength of the epidemiologic evidence for carcinogenicity depends, among other things, on the type of analysis and on the magnitude and specificity of the response. The weight of evidence increases rapidly with the number of adequate studies that show comparable results on populations exposed to the same agent under different conditions.

It should be recognized that epidemiologic studies are inherently capable of detecting only comparatively large increases in the relative risk of

[51 FR 33996]

cancer. Negative results from such studies cannot prove the absence of carcinogenic action; however, negative results from a well-designed and well-conducted epidemiologic study that contains usable exposure data can serve to define upper limits of risk; these are useful if animal evidence indicates that the agent is potentially carcinogenic in humans.

C. Weight of Evidence

Evidence of possible carcinogenicity in humans comes primarily from two sources: long-term animal tests and epidemiologic investigations. Results from these studies are supplemented with available information from short-term tests, pharmacokinetic studies, comparative metabolism studies, structure-activity relationships, and other relevant toxicologic studies. The question of how likely an agent is to be a human carcinogen should be answered in the framework of a weight-of-evidence judgment. Judgments about the weight of evidence involve considerations of the quality and adequacy of the data and the kinds and consistency of responses induced by a suspect carcinogen. There are three major steps to characterizing the weight of evidence for carcinogenicity in humans: (1) characterization of the evidence from human studies and from animal studies individually, (2) combination of the characterizations of these two types of data into an indication of the overall weight of evidence for human carcinogenicity, and (3) evaluation of all supporting information to determine if the overall weight of evidence should be modified.

EPA has developed a system for stratifying the weight of evidence (see section IV). This classification is not meant to be applied rigidly or mechanically. At various points in the above discussion, EPA has emphasized the need for an overall, balanced judgment of the totality of the available evidence. Particularly for well-studied substances, the scientific data base will have a complexity that cannot be captured by any classification scheme. Therefore, the hazard identification section should include a narrative summary of the strengths and weaknesses of the evidence as well as its categorization in the EPA scheme.

The EPA classification system is, in general, an adaptation of the International Agency for Research on Cancer (IARC, 1982) approach for classifying the

weight of evidence for human data and animal data. The EPA classification system for the characterization of the overall weight of evidence for carcinogenicity (animal, human, and other supportive data) includes: Group A -- Carcinogenic to Humans; Group B -- Probably Carcinogenic to Humans; Group C -- Possibly Carcinogenic to Humans; Group D -- Not Classifiable as to Human Carcinogenicity; and Group E -- Evidence of Non-Carcinogenicity for Humans.

The following modifications of the IARC approach have been made for classifying human and animal studies.

For human studies:

(1) The observation of a statistically significant association between an agent and life-threatening benign tumors in humans is included in the evaluation of risks to humans.

(2) A "no data available" classification is added.

(3) A "no evidence of carcinogenicity" classification is added. This classificaton indicates that no association was found between exposure and increased risk of cancer in well-conducted, well-designed, independent analytical epidemiologic studies.

For animal studies:

(1) An increased incidence of combined benign and malignant tumors will be considered to provide sufficient evidence of carcinogenicity if the other criteria defining the "sufficient" classification of evidence are met (e.g., replicate studies, malignancy; see section IV). Benign and malignant tumors will be combined when scientifically defensible.

(2) An increased incidence of benign tumors alone generally constitutes "limited" evidence of carcinogenicity.

(3) An increased incidence of neoplasms that occur with high spontaneous background incidence (e.g., mouse liver tumors and rat pituitary tumors in certain strains) generally constitutes "sufficient" evidence of carcinogenicity, but may be changed to "limited" when warranted by the specific information available on the agent.

(4) A "no data available" classification has been added.

(5) A "no evidence of carcinogenicity" classification is also added. This operational classification would include substances for which there is no increased incidence of neoplasms in at least two well-designed and well-conducted animal studies of adequate power and dose in different species.

D. Guidance for Dose-Response Assessment

The qualitative evidence for carcinogenesis should be discussed for purposes of guiding the dose-response assessment. The guidance should be given in terms of the appropriateness and limitations of specific studies as well as pharmacokinetic considerations that should be factored into the dose-response assessment. The appropriate method of extrapolation should be factored in when the experimental route of exposure differs from that occurring in humans.

Agents that are judged to be in the EPA weight-of-evidence stratification Groups A and B would be regarded as suitable for quantitative risk assessments. Agents that are judged to be in Group C will generally be regarded as suitable for quantitative risk assessment, but judgments in this regard may be made on a case-by-case basis. Agents that are judged to be in Groups D and E would not have quantitative risk assessments.

E. Summary and Conclusion

The summary should present all of the key findings in all of the sections of the qualitative assessment and the interpretive rationale that forms the basis for the conclusion. Assumptions, uncertainties in the evidence, and other factors that may affect the relevance of the evidence to humans should be discussed. The conclusion should present both the weight-of-evidence ranking and a description that brings out the more subtle aspects of the evidence that may not be evident from the ranking alone.

III. Dose-Response Assessment, Exposure Assessment, and Risk Characterization

After data concerning the carcinogenic properties of a substance have been collected, evaluated, and categorized, it is frequently desirable to estimate the likely range of excess cancer risk associated with given levels and conditions of human exposure. The first step of the analysis needed to make such estimations is the development of the likely relationship between dose and response (cancer incidence) in the region of human exposure. This information on dose-response relationships is coupled with information on the nature and magnitude of human exposure to yield an estimate of human risk. The risk-characterization step also includes an interpretation of these estimates in light of the biological, statistical, and exposure assumptions and uncertainties that have arisen throughout the process of assessing risk.

The elements of dose-response assessment are described in section III.A. Guidance on human exposure assessment is provided in another EPA

[51 FR 33997]

document (U.S. EPA, 1986); however, section III.B. of these Guidelines includes a brief description of the specific type of exposure information that is useful for carcinogen risk assessment. Finally, in section III.C. on risk characterization, there is a description of the manner in which risk estimates should be presented so as to be most informative.

It should be emphasized that calculation of quantitative estimates of cancer risk does not

require that an agent be carcinogenic in humans. The likelihood that an agent is a human carcinogen is a function of the weight of evidence, as this has been described in the hazard identification section of these Guidelines. It is nevertheless important to present quantitative estimates, appropriately qualified and interpreted, in those circumstances in which there is a reasonable possibility, based on human and animal data, that the agent is carcinogenic in humans.

It should be emphasized in every quantitative risk estimation that the results are uncertain. Uncertainties due to experimental and epidemiologic variability as well as uncertainty in the exposure assessment can be important. There are major uncertainties in extrapolating both from animals to humans and from high to low doses. There are important species differences in uptake, metabolism, and organ distribution of carcinogens, as well as species and strain differences in target-site susceptibility. Human populations are variable with respect to genetic constitution, diet, occupational and home environment, activity patterns, and other cultural factors. Risk estimates should be presented together with the associated hazard assessment (section III.C.3.) to ensure that there is an appreciation of the weight of evidence for carcinogenicity that underlies the quantitative risk estimates.

A. Dose-Response Assessment

1. *Selection of Data.* As indicated in section II.D., guidance needs to be given by the individuals doing the qualitative assessment (toxicologists, pathologists, pharmacologists, etc.) to those doing the quantitative assessment as to the appropriate data to be used in the dose-response assessment. This is determined by the quality of the data, its relevance to human modes of exposure, and other technical details.

If available, estimates based on adequate human epidemiologic data are preferred over estimates based on animal data. If adequate exposure data exist in a well-designed and well-conducted negative epidemiologic study, it may be possible to obtain an upper-bound estimate of risk from that study. Animal-based estimates, if available, also should be presented.

In the absence of appropriate human studies, data from a species that responds most like humans should be used, if information to this effect exists. Where, for a given agent, several studies are available, which may involve different animal species, strains, and sexes at several doses and by different routes of exposure, the following approach to selecting the data sets is used: (1) The tumor incidence data are separated according to organ site and tumor type. (2) All biologically and statistically acceptable data sets are presented. (3) The range of the risk estimates is presented with due regard to biological relevance (particularly in the case of animal studies) and appropriateness of route of exposure. (4) Because it is possible that human sensitivity is as high as the most sensitive responding animal species, in the absence of evidence to the contrary, the biologically acceptable data set from long-term animal studies showing the greatest sensitivity should generally be given the greatest emphasis, again with due regard to biological and statistical considerations.

When the exposure route in the species from which the dose-response information is obtained differs from the route occurring in environmental exposures, the considerations used in making the route-to-route extrapolation must be carefully described. All assumptions should be presented along with a discussion of the uncertainties in the extrapolation. Whatever procedure is adopted in a given case, it must be consistent with the existing metabolic and pharmacokinetic information on the chemical (e.g., absorption efficiency via the gut and lung, target organ doses, and changes in placental transport throughout gestation for transplacental carcinogens).

Where two or more significantly elevated tumor sites or types are observed in the same study, extrapolations may be conducted on selected sites or types. These selections will be made on biological grounds. To obtain a total estimate of carcinogenic risk, animals with one or more tumor sites or types showing significantly elevated tumor incidence should be pooled and used for extrapolation. The pooled estimates will generally be used in preference to risk estimates based on single sites or types. Quantitative risk extrapolations will generally not be done on the basis of totals that include tumor sites without statistically significant elevations.

Benign tumors should generally be combined with malignant tumors for risk estimates unless the benign tumors are not considered to have the potential to progress to the associated malignancies of the same histogenic origin. The contribution of the benign tumors, however, to the total risk should be indicated.

2. *Choice of Mathematical Extrapolation Model.* Since risks at low exposure levels cannot be measured directly either by animal experiments or by epidemiologic studies, a number of mathematical models have been developed to extrapolate from high to low dose. Different extrapolation models, however, may fit the observed data reasonably well but may lead to large differences in the projected risk at low doses.

As was pointed out by OSTP (1985; Principle 26),

> No single mathematical procedure is recognized as the most appropriate for low-dose extrapolation in carcinogenesis. When relevant biological evidence on mechanism of action exists (e.g., pharmacokinetics, target organ dose), the models or procedures

employed should be consistent with the evidence. When data and information are limited, however, and when much uncertainty exists regarding the mechanism of carcinogenic action, models or procedures which incorporate low-dose linearity are preferred when compatible with the limited information.

At present, mechanisms of the carcinogenesis process are largely unknown and data are generally limited. If a carcinogenic agent acts by accelerating the same carcinogenic process that leads to the background occurrence of cancer, the added effect of the carcinogen at low doses is expected to be virtually linear (Crump et al., 1976).

The Agency will review each assessment as to the evidence on carcinogenesis mechanisms and other biological or statistical evidence that indicates the suitability of a particular extrapolation model. Goodness-of-fit to the experimental observations is not an effective means of discriminating among models (OSTP, 1985). A rationale will be included to justify the use of the chosen model. In the absence of adequate information to the contrary, the linearized multistage procedure will be employed. Where appropriate, the results of using various extrapolation models may be useful for comparison with the linearized multistage procedure. When longitudinal data on tumor development are available, time-to-tumor models may be used.

It should be emphasized that the linearized multistage procedure leads to

[51 FR 33998]

a plausible upper limit to the risk that is consistent with some proposed mechanisms of carcinogenesis. Such an estimate, however, does not necessarily give a realistic prediction of the risk. The true value of the risk is unknown, and may be as low as zero. The range of risks, defined by the upper limit given by the chosen model and the lower limit which may be as low as zero, should be explicitly stated. An established procedure does not yet exist for making "most likely" or "best" estimates of risk within the range of uncertainty defined by the upper and lower limit estimates. If data and procedures become available, the Agency will also provide "most likely" or "best" estimates of risk. This will be most feasible when human data are available and when exposures are in the dose range of the data.

In certain cases, the linearized multistage procedure cannot be used with the observed data as, for example, when the data are nonmonotonic or flatten out at high doses. In these cases, it may be necessary to make adjustments to achieve low-dose linearity.

When pharmacokinetic or metabolism data are available, or when other substantial evidence on the mechanistic aspects of the carcinogenesis process exists, a low-dose extrapolation model other than the linearized multistage procedure might be considered more appropriate on biological grounds. When a different model is chosen, the risk assessment should clearly discuss the nature and weight of evidence that led to the choice. Considerable uncertainty will remain concerning response at low doses; therefore, in most cases an upper-limit risk estimate using the linearized multistage procedure should also be presented.

3. *Equivalent Exposure Units Among Species.* Low-dose risk estimates derived from laboratory animal data extrapolated to humans are complicated by a variety of factors that differ among species and potentially affect the response to carcinogens. Included among these factors are differences between humans and experimental test animals with respect to life span, body size, genetic variability, population homogeneity, existence of concurrent disease, pharmacokinetic effects such as metabolism and excretion patterns, and the exposure regimen.

The usual approach for making interspecies comparisons has been to use standardized scaling factors. Commonly employed standardized dosage scales include mg per kg body weight per day, ppm in the diet or water, mg per m^2 body surface area per day, and mg per kg body weight per lifetime. In the absence of comparative toxicological, physiological, metabolic, and pharmacokinetic data for a given suspect carcinogen, the Agency takes the position that the extrapolation on the basis of surface area is considered to be appropriate because certain pharmacological effects commonly scale according to surface area (Dedrick, 1973; Freireich et al., 1966; Pinkel, 1958).

B. Exposure Assessment

In order to obtain a quantitative estimate of the risk, the results of the dose-response assessment must be combined with an estimate of the exposures to which the populations of interest are likely to be subject. While the reader is referred to the Guidelines for Estimating Exposures (U.S. EPA, 1986) for specific details, it is important to convey an appreciation of the impact of the strengths and weaknesses of exposure assessment on the overall cancer risk assessment process.

At present there is no single approach to exposure assessment that is appropriate for all cases. On a case-by-case basis, appropriate methods are selected to match the data on hand and the level of sophistication required. The assumptions, approximations, and uncertainties need to be clearly stated because, in some instances, these will have a major effect on the risk assessment.

In general, the magnitude, duration, and frequency of exposure provide fundamental information for estimating the concentration of the carcinogen to which the organism is exposed. These data are generated from monitoring information, modeling results, and/or reasoned estimates. An appropriate treatment of exposure should consider

the potential for exposure via ingestion, inhalation, and dermal penetration from relevant sources of exposures including multiple avenues of intake from the same source.

Special problems arise when the human exposure situation of concern suggests exposure regimens, e.g., route and dosing schedule that are substantially different from those used in the relevant animal studies. Unless there is evidence to the contrary in a particular case, the cumulative dose received over a lifetime, expressed as average daily exposure prorated over a lifetime, is recommended as an appropriate measure of exposure to a carcinogen. That is, the assumption is made that a high dose of a carcinogen received over a short period of time is equivalent to a corresponding low dose spread over a lifetime. This approach becomes more problematical as the exposures in question become more intense but less frequent, especially when there is evidence that the agent has shown dose-rate effects.

An attempt should be made to assess the level of uncertainty associated with the exposure assessment which is to be used in a cancer risk assessment. This measure of uncertainty should be included in the risk characterization (section III.C.) in order to provide the decision-maker with a clear understanding of the impact of this uncertainty on any final quantitative risk estimate. Subpopulations with heightened susceptibility (either because of exposure or predisposition) should, when possible, be identified.

C. Risk Characterization

Risk characterization is composed of two parts. One is a presentation of the numerical estimates of risk; the other is a framework to help judge the significance of the risk. Risk characterization includes the exposure assessment and dose-response assessment; these are used in the estimation of carcinogenic risk. It may also consist of a unit-risk estimate which can be combined elsewhere with the exposure assessment for the purposes of estimating cancer risk.

Hazard identification and dose-response assessment are covered in sections II. and III.A., and a detailed discussion of exposure assessment is contained in EPA's Guidelines for Estimating Exposures (U.S. EPA, 1986). This section deals with the numerical risk estimates and the approach to summarizing risk characterization.

1. *Options for Numerical Risk Estimates.* Depending on the needs of the individual program offices, numerical estimates can be presented in one or more of the following three ways.

a. Unit Risk -- Under an assumption of low-dose linearity, the unit cancer risk is the excess lifetime risk due to a continuous constant lifetime exposure of one unit of carcinogen concentration. Typical exposure units include ppm or ppb in food or water, mg/kg/day by ingestion, or ppm or $\mu g/m^3$ in air.

b. Dose Corresponding to a Given Level of Risk -- This approach can be useful, particularly when using nonlinear extrapolation models where the unit risk would differ at different dose levels.

c. Individual and Population Risks -- Risks may be characterized either in terms of the excess individual lifetime risks, the excess number of cancers

[51 FR 33999]

produced per year in the exposed population, or both.

Irrespective of the options chosen, the degree of precision and accuracy in the numerical risk estimates currently do not permit more than one significant figure to be presented.

2. *Concurrent Exposure.* In characterizing the risk due to concurrent exposure to several carcinogens, the risks are combined on the basis of additivity unless there is specific information to the contrary. Interactions of cocarcinogens, promoters, and inititators with known carcinogens should be considered on a case-by-case basis.

3. *Summary of Risk Characterization.* Whichever method of presentation is chosen, it is critical that the numerical estimates not be allowed to stand alone, separated from the various assumptions and uncertainties upon which they are based. The risk characterization should contain a discussion and interpretation of the numerical estimates that affords the risk manager some insight into the degree to which the quantitative estimates are likely to reflect the true magnitude of human risk, which generally cannot be known with the degree of quantitative accuracy reflected in the numerical estimates. The final risk estimate will be generally rounded to one significant figure and will be coupled with the EPA classification of the qualitative weight of evidence. For example, a lifetime individual risk of 2×10^{-4} resulting from exposure to a "probable human carcinogen" (Group B2) should be designated as 2×10^{-4} [B2] . This bracketed designation of the qualitative weight of evidence should be included with all numerical risk estimates (i.e., unit risks, which are risks at a specified concentration or concentrations corresponding to a given risk). Agency statements, such as *FEDERAL REGISTER* notices, briefings, and action memoranda, frequently include numerical estimates of carcinogenic risk. It is recommended that whenever these numerical estimates are used, the qualitative weight-of-evidence classification should also be included.

The section on risk characterization should summarize the hazard identification, dose-response assessment, exposure assessment, and the public health risk estimates. Major assumptions, scientific judgments, and, to the extent possible, estimates of

the uncertainties embodied in the assessment are presented.

IV. EPA Classification System for Categorizing Weight of Evidence for Carcinogenicity from Human and Animal Studies (Adapted from IARC)

A. Assessment of Weight of Evidence for Carcinogenicity from Studies in Humans

Evidence of carcinogenicity from human studies comes from three main sources:

1. Case reports of individual cancer patients who were exposed to the agent(s).
2. Descriptive epidemiologic studies in which the incidence of cancer in human populations was found to vary in space or time with exposure to the agent(s).
3. Analytical epidemiologic (case-control and cohort) studies in which individual exposure to the agent(s) was found to be associated with an increased risk of cancer.

Three criteria must be met before a causal association can be inferred between exposure and cancer in humans:

1. There is no identified bias that could explain the association.
2. The possibility of confounding has been considered and ruled out as explaining the association.
3. The association is unlikely to be due to chance.

In general, although a single study may be indicative of a cause-effect relationship, confidence in inferring a causal association is increased when several independent studies are concordant in showing the association, when the association is strong, when there is a dose-response relationship, or when a reduction in exposure is followed by a reduction in the incidence of cancer.

The weight of evidence for carcinogenicity[1] from studies in humans is classified as:

1. Sufficient evidence of carcinogenicity, which indicates that there is a causal relationship between the agent and human cancer.
2. Limited evidence of carcinogenicity, which indicates that a causal interpretation is credible, but that alternative explanations, such as chance, bias, or confounding, could not adequately be excluded.
3. Inadequate evidence, which indicates that one of two conditions prevailed: (a) there were few pertinent data, or (b) the available studies, while showing evidence of association, did not exclude chance, bias, or confounding, and therefore a causal interpretation is not credible.
4. No data, which indicates that data are not available.
5. No evidence, which indicates that no association was found between exposure and an increased risk of cancer in well-designed and well-conducted independent analytical epidemiologic studies.

B. Assessment of Weight of Evidence for Carcinogenicity from Studies in Experimental Animals

These assessments are classified into five groups:

1. Sufficient evidence[2] of carcinogenicity, which indicates that there is an increased incidence of malignant tumors or combined malignant and benign tumors:[3] (a) in multiple species or strains; or (b) in multiple experiments (e.g., with different routes of administration or using different dose levels); or (c) to an unusual degree in a single experiment with regard to high incidence, unusual site or type of tumor, or early age at onset.

Additional evidence may be provided by data on dose-response effects, as well as information from short-term tests or on chemical structure.

2. Limited evidence of carcinogenicity, which means that the data suggest a carcinogenic effect but are limited because: (a) the studies involve a single species, strain, or experiment and do not meet criteria for sufficient evidence (see section IV. B.1.c); (b) the experiments are restricted by inadequate dosage levels, inadequate duration of exposure to the agent, inadequate period of follow-up, poor survival, too few animals, or inadequate reporting; or (c) an increase in the incidence of benign tumors only.
3. Inadequate evidence, which indicates that because of major qualitative or quantitative limitations, the studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect.
4. No data, which indicates that data are not available.
5. No evidence, which indicates that there is no increased incidence of neoplasms in at least two well-designed

[51 FR 34000]

and well-conducted animal studies in different species.

The classifications "sufficient evidence" and "limited evidence" refer only to the weight of the experimental evidence that these agents are carcinogenic and not to the potency of their carcinogenic action.

[1] For purposes of public health protection, agents associated with life-threatening benign tumors in humans are included in the evaluation.

[2] An increased incidence of neoplasms that occur with high spontaneous background incidence (e.g., mouse liver tumors and rat pituitary tumors in certain strains) generally constitutes "sufficient" evidence of carcinogenicity, but may be changed to "limited" when warranted by the specific information available on the agent.

[3] Benign and malignant tumors will be combined unless the benign tumors are not considered to have the potential to progress to the associated malignancies of the same histogenic origin.

C. Categorization of Overall Weight of Evidence for Human Carcinogenicity

The overall scheme for categorization of the weight of evidence of carcinogenicity of a chemical for humans uses a three-step process. (1) The weight of evidence in human studies or animal studies is summarized; (2) these lines of information are combined to yield a tentative assignment to a category (see Table 1); and (3) all relevant supportive information is evaluated to see if the designation of the overall weight of evidence needs to be modified. Relevant factors to be included along with the tumor information from human and animal studies include structure-activity relationships; short-term test findings; results of appropriate physiological, biochemical, and toxicological observations; and comparative metabolism and pharmacokinetic studies. The nature of these findings may cause one to adjust the overall categorization of the weight of evidence.

The agents are categorized into five groups as follows:

Group A -- Human Carcinogen

This group is used only when there is sufficient evidence from epidemiologic studies to support a causal association between exposure to the agents and cancer.

Group B -- Probable Human Carcinogen

This group includes agents for which the weight of evidence of human carcinogenicity based on epidemiologic studies is "limited" and also includes agents for which the weight of evidence of carcinogenicity based on animal studies is "sufficient." The group is divided into two subgroups. Usually, Group B1 is reserved for agents for which there is limited evidence of carcinogenicity from epidemiologic studies. It is reasonable, for practical purposes, to regard an agent for which there is "sufficient" evidence of carcinogenicity in animals as if it presented a carcinogenic risk to humans. Therefore, agents for which there is "sufficient" evidence from animal studies and for which there is "inadequate evidence" or "no data" from epidemiologic studies would usually be categorized under Group B2.

Group C -- Possible Human Carcinogen

This group is used for agents with limited evidence of carcinogenicity in animals in the absence of human data. It includes a wide variety of evidence, e.g., (a) a malignant tumor response in a single well-conducted experiment that does not meet conditions for sufficient evidence, (b) tumor responses of marginal statistical significance in studies having inadequate design or reporting, (c) benign but not malignant tumors with an agent showing no response in a variety of short-term tests for mutagenicity, and (d) responses of marginal statistical significance in a tissue known to have a high or variable background rate.

Group D -- Not Classifiable as to Human Carcinogenicity

This group is generally used for agents with inadequate human and animal evidence of carcinogenicity or for which no data are available.

Group E -- Evidence of Non-Carcinogenicity for Humans

This group is used for agents that show no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiologic and animal studies.

The designation of an agent as being in Group E is based on the available evidence and should not be interpreted as a definitive conclusion that the agent will not be a carcinogen under any circumstances.

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TABLE 1.--ILLUSTRATIVE CATEGORIZATION OF EVIDENCE BASED ON ANIMAL AND HUMAN DATA[1]

Human evidence	Animal evidence				
	Sufficient	Limited	Inadequate	No data	No evidence
Sufficient	A	A	A	A	A
Limited	B1	B1	B1	B1	B1
Inadequate	B2	C	D	D	D
No data	B2	C	D	D	E
No evidence	B2	C	D	D	E

1 The above assignments are presented for illustrative purposes. There may be nuances in the classification of both animal and human data indicating that different categorizations than those given in the table should be assigned. Furthermore, these assignments are tentative and may be modified by ancillary evidence. In this regard all relevant information should be evaluated to determine if the designation of the overall weight of evidence needs to be modified. Relevant factors to be included along with the tumor data from human and animal studies include structure-activity relationships, short-term test findings, results of appropriate physiological, biochemical, and toxicological observations, and comparative metabolism and pharmacokinetic studies. The nature of these findings may cause an adjustment of the overall categorization of the weight of evidence.

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Part B: Response to Public and Science Advisory Board Comments

I. Introduction

This section summarizes the major issues raised during both the public comment period on the Proposed Guidelines for Carcinogen Risk Assessment published on November 23, 1984 (49 FR 46294), and also during the April 22-23, 1985, meeting of the Carcinogen Risk Assessment Guidelines Panel of the Science Advisory Board (SAB).

In order to respond to these issues the Agency modified the proposed guidelines in two stages. First, changes resulting from consideration of the public comments were made in a draft sent to the SAB review panel prior to their April meeting. Secondly, the guidelines were further modified in response to the panel's recommendations.

The Agency received 62 sets of comments during the public comment period, including 28 from corporations, 9 from professional or trade associations, and 4 from academic institutions. In general, the comments were favorable. The commentors welcomed the update of the 1976 guidelines and felt that the proposed guidelines of

1985 reflected some of the progress that has occurred in understanding the mechanisms of carcinogenesis. Many commentors, however, felt that additional changes were warranted.

The SAB concluded that the guidelines are "reasonably complete in their conceptual framework and are sound in their overall interpretation of the scientific issues" (Report by the SAB Carcinogenicity Guidelines Review Group, June 19, 1985). The SAB suggested various editorial changes and raised some issues regarding the content of the proposed guidelines, which are discussed below. Based on these recommendations, the Agency has modified the draft guidelines.

II. Office of Science and Technology Policy Report on Chemical Carcinogens

Many commentors requested that the final guidelines not be issued until after publication of the report of the Office of Technology and Science Policy (OSTP) on chemical carcinogens. They further requested that this report be incorporated into the final Guidelines for Carcinogen Risk Assessment.

The final OSTP report was published in 1985 (50 FR 10372). In its deliberations, the Agency reviewed the final OSTP report and feels that the Agency's guidelines are consistent with the principles established by the OSTP. In its review, the SAB agreed that the Agency guidelines are generally consistent with the OSTP report. To emphasize this consistency, the OSTP principles have been incorporated into the guidelines when controversial issues are discussed.

III. Inference Guidelines

Many commentors felt that the proposed guidelines did not provide a sufficient distinction between scientific fact and policy decisions. Others felt that EPA should not attempt to propose firm guidelines in the absence of scientific consensus. The SAB report also indicated the need to "distinguish recommendations based on scientific evidence from those based on science policy decisions."

The Agency agrees with the recommendation that policy, judgmental, or inferential decisions should be clearly identified. In its revision of the proposed guidelines, the Agency has included phrases (e.g., "the Agency takes the position that") to more clearly distinguish policy decisions.

The Agency also recognizes the need to establish procedures for action on important issues in the absence of complete scientific knowledge or consensus. This need was acknowledged in both the National Academy of Sciences book entitled *Risk Management in the Federal Government: Managing the Process* and the OSTP report on chemical carcinogens. As the NAS report states, "Risk assessment is an analytic process that is firmly based on scientific considerations, but it also requires judgments to be made when the available information is incomplete. These judgments inevitably draw on both scientific and policy considerations."

[51 FR 34002]

The judgments of the Agency have been based on current available scientific information and on the combined experience of Agency experts. These judgments, and the resulting guidance, rely on inference; however, the positions taken in these inference guidelines are felt to be reasonable and scientifically defensible. While all of the guidance is, to some degree, based on inference, the guidelines have attempted to distinguish those issues that depended more on judgment. In these cases, the Agency has stated a position but has also retained flexibility to accommodate new data or specific circumstances that demonstrate that the proposed position is inaccurate. The Agency recognizes that scientific opinion will be divided on these issues.

Knowledge about carcinogens and carcinogenesis is progressing at a rapid rate. While these guidelines are considered a best effort at the present time, the Agency has attempted to incorporate flexibility into the current guidelines and also recommends that the guidelines be revised as often as warranted by advances in the field.

IV. Evaluation of Benign Tumors

Several commentors discussed the appropriate interpretation of an increased incidence of benign tumors alone or with an increased incidence of malignant tumors as part of the evaluation of the carcinogenicity of an agent. Some comments were supportive of the position in the proposed guidelines, i.e., under certain circumstances, the incidence of benign and malignant tumors would be combined, and an increased incidence of benign tumors alone would be considered an indication, albeit limited, of carcinogenic potential. Other commentors raised concerns about the criteria that would be used to decide which tumors should be combined. Only a few commentors felt that benign tumors should never be considered in evaluating carcinogenic potential.

The Agency believes that current information supports the use of benign tumors. The guidelines have been modified to incorporate the language of the OSTP report, i.e., benign tumors will be combined with malignant tumors when scientifically defensible. This position allows flexibility in evaluating the data base for each agent. The guidelines have also been modified to indicate that, whenever benign and malignant tumors have been combined, and the agent is considered a candidate for quantitative risk extrapolation, the contribution of benign tumors to the estimation of risk will be indicated.

V. *Transplacental and Multigenerational Animal Bioassays*

As one of its two proposals for additions to the guidelines, the SAB recommended a discussion of transplacental and multigenerational animal bioassays for carcinogenicity.

The Agency agrees that such data, when available, can provide useful information in the evaluation of a chemical's potential carcinogenicity and has stated this in the final guidelines. The Agency has also revised the guidelines to indicate that such studies may provide additional information on the metabolic and pharmacokinetic properties of the chemical. More guidance on the specific use of these studies will be considered in future revisions of these guidelines.

VI. Maximum Tolerated Dose

The proposed guidelines discussed the implications of using a maximum tolerated dose (MTD) in bioassays for carcinogenicity. Many commentors requested that EPA define MTD. The tone of the comments suggested that the commentors were concerned about the uses and interpretations of high-dose testing.

The Agency recognizes that controversy currently surrounds these issues. The appropriate text from the OSTP report has been incorporated into the final guidelines which suggests that the consequences of high-dose testing be evaluated on a case-by-case basis.

VII. Mouse Liver Tumors

A large number of commentors expressed opinions about the assessment of bioassays in which the only increase in tumor incidence was liver tumors in the mouse. Many felt that mouse liver tumors were afforded too much credence, especially given existing information that indicates that they might arise by a different mechanism, e.g., tissue damage followed by regeneration. Others felt that mouse liver tumors were but one case of a high background incidence of one particular type of tumor and that all such tumors should be treated in the same fashion.

The Agency has reviewed these comments and the OSTP principle regarding this issue. The OSTP report does not reach conclusions as to the treatment of tumors with a high spontaneous background rate, but states, as is now included in the text of the guidelines, that these data require special consideration. Although questions have been raised regarding the validity of mouse liver tumors in general, the Agency feels that mouse liver tumors cannot be ignored as an indicator of carcinogenicity. Thus, the position in the proposed guidelines has not been changed: an increased incidence of only mouse liver tumors will be regarded as "sufficient" evidence of carcinogenicity if all other criteria, e.g., replication and malignancy, are met with the understanding that this classification could be changed to "limited" if warranted. The factors that may cause this re-evaluation are indicated in the guidelines.

VIII. Weight-of Evidence Catagories

The Agency was praised by both the public and the SAB for incorporating a weight-of-evidence scheme into its evaluation of carcinogenic risk. Certain specific aspects of the scheme, however, were criticized.

1. Several commentors noted that while the text of the proposed guidelines clearly states that EPA will use all available data in its categorization of the weight of the evidence that a chemical is a carcinogen, the classification system in Part A, section IV did not indicate the manner in which EPA will use information other than data from humans and long-term animal studies in assigning a weight-of-evidence classification.

The Agency has added a discussion to Part A, section IV.C. dealing with the characterization of overall evidence for human carcinogenicity. This discussion clarifies EPA's use of supportive information to adjust, as warranted, the designation that would have been made solely on the basis of human and long-term animal studies.

2. The Agency agrees with the SAB and those commentors who felt that a simple classification of the weight of evidence, e.g., a single letter or even a descriptive title, is inadequate to describe fully the weight of evidence for each individual chemical. The final guidelines propose that a paragraph summarizing the data should accompany the numerical estimate and weight-of-evidence classification whenever possible.

3. Several commentors objected to the descriptive title E (No Evidence of Carcinogenicity for Humans) because they felt the title would be confusing to people inexperienced with the classification system. The title for Group E, No Evidence of Carcinogenicity for Humans, was thought by these commentors to suggest the absence of data. This group, however, is intended to be reserved for agents for which there exists credible data demonstrating that the agent is not carcinogenic.

Based on these comments and further discussion, the Agency has changed the

[51 FR 34003]

title of Group E to "Evidence of Non-Carcinogenicity for Humans."

4. Several commentors felt that the title for Group C, Possible Human Carcinogen, was not sufficiently distinctive from Group B, Probable Human Carcinogen. Other commentors felt that those agents that minimally qualified for Group C would lack sufficient data for such a label.

The Agency recognizes that Group C covers a range of chemicals and has considered whether to subdivide Group C. The consensus of the Agency's

Carcinogen Risk Assessment Committee, however, is that the current groups, which are based on the IARC categories, are a reasonable stratification and should be retained at present. The structure of the groups will be reconsidered when the guidelines are reviewed in the future. The Agency also feels that the descriptive title it originally selected best conveys the meaning of the classification within the context of EPA's past and current activities.

5. Some commentors indicated a concern about the distinction between B1 and B2 on the basis of epidemiologic evidence only. This issue has been under discussion in the Agency and may be revised in future versions of the guidelines.

6. Comments were also received about the possibility of keeping the groups for animal and human data separate without reaching a combined classification. The Agency feels that a combined classification is useful; thus, the combined classification was retained in the final guidelines.

The SAB suggested that a table be added to Part A, section IV to indicate the manner in which human and animal data would be combined to obtain an overall weight-of-evidence category. The Agency realizes that a table that would present all permutations of potentially available data would be complex and possibly impossible to construct since numerous combinations of ancillary data (e.g., genetic toxicity, pharmacokinetics) could be used to raise or lower the weight-of-evidence classification. Nevertheless, the Agency decided to include a table to illustrate the most probable weight-of-evidence classification that would be assigned on the basis of standard animal and human data without consideration of the ancillary data. While it is hoped that this table will clarify the weight-of-evidence classifications, it is also important to recognize that an agent may be assigned to a final categorization different from the category which would appear appropriate from the table and still conform to the guidelines.

IX. Quantitative Estimates of Risk

The method for quantitative estimates of carcinogenic risk in the proposed guidelines received substantial comments from the public. Five issues were discussed by the Agency and have resulted in modifications of the guidelines.

1. The major criticism was the perception that EPA would use only one method for the extrapolation of carcinogenic risk and would, therefore, obtain one estimate of risk. Even commentors who concur with the procedure usually followed by EPA felt that some indication of the uncertainty of the risk estimate should be included with the risk estimate.

The Agency feels that the proposed guidelines were not intended to suggest that EPA would perform quantitative risk estimates in a rote or mechanical fashion. As indicated by the OSTP report and paraphrased in the proposed guidelines, no single mathematical procedure has been determined to be the most appropriate method for risk extrapolation. The final guidelines quote rather than paraphrase the OSTP principle. The guidelines have been revised to stress the importance of considering all available data in the risk assessment and now state, "The Agency will review each assessment as to the evidence on carcinogenic mechanisms and other biological or statistical evidence that indicates the suitability of a particular extrapolation model." Two issues are emphasized: First, the text now indicates the potential for pharmacokinetic information to contribute to the assessment of carcinogenic risk. Second, the final guidelines state that time-to-tumor risk extrapolation models may be used when longitudinal data on tumor development are available.

2. A number of commentors noted that the proposed guidelines did not indicate how the uncertainties of risk characterization would be presented. The Agency has revised the proposed guidelines to indicate that major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties embodied in the risk assessment will be presented along with the estimation of risk.

3. The proposed guidelines stated that the appropriateness of quantifying risks for chemicals in Group C (Possible Human Carcinogen), specifically those agents that were on the boundary of Groups C and D (Not Classifiable as to Human Carcinogenicity), would be judged on a case-by-case basis. Some commentors felt that quantitative risk assessment should not be performed on any agent in Group C.

Group C includes a wide range of agents, including some for which there are positive results in one species in one good bioassay. Thus, the Agency feels that many agents in Group C will be suitable for quantitative risk assessment, but that judgments in this regard will be made on a case-by-case basis.

4. A few commentors felt that EPA intended to perform quantitative risk estimates on aggregate tumor incidence. While EPA will consider an increase in total aggregate tumors as suggestive of potential carcinogenicity, EPA does not generally intend to make quantitative estimates of carcinogenic risk based on total aggregate tumor incidence.

5. The proposed choice of body surface area as an interspecies scaling factor was criticized by several commentors who felt that body weight was also appropriate and that both methods should be used. The OSTP report recognizes that both scaling factors are in common use. The Agency feels that the choice of the body surface area scaling factor can be

justified from the data on effects of drugs in various species. Thus, EPA will continue to use this scaling factor unless data on a specific agent suggest that a different scaling factor is justified. The uncertainty engendered by choice of scaling factor will be included in the summary of uncertainties associated with the assessment of risk mentioned in point 1, above.

In the second of its two proposals for additions to the proposed guidelines, the SAB suggested that a sensitivity analysis be included in EPA's quantitative estimate of a chemical's carcinogenic potency. The Agency agrees that an analysis of the assumptions and uncertainties inherent in an assessment of carcinogenic risk must be accurately portrayed. Sections of the final guidelines that deal with this issue have been strengthened to reflect the concerns of the SAB and the Agency. In particular, the last paragraph of the guidelines states that "major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties embodied in the assessment" should be presented in the summary characterizing the risk. Since the assumptions and uncertainties will vary for each assessment, the Agency feels that a formal requirement for a particular type of sensitivity analysis would be less useful than a case-by-case evaluation of the particular assumptions and uncertainties most significant for a particular risk assessment.

51 FR 34006

GUIDELINES FOR MUTAGENICITY RISK ASSESSMENT

SUMMARY: On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for Mutagenicity Risk Assessment.

The Guidelines for Mutagenicity Risk Assessment (hereafter "Guidelines") are intended to guide Agency analysis of mutagenicity data in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for Mutagenicity Risk Assessment published November 23, 1984 (49 FR 46314).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

FOR FURTHER INFORMATION CONTACT:

Dr. Lawrence R. Valcovic
Reproductive Effects Assessment Group
Office of Health and Environmental Assessment
(RD-689)
U. S. Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460
202-382-7303

SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process*. In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for Mutagenicity Risk Assessment

Work on the Guidelines for Mutagenicity Risk Assessment began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the field of genetic toxicology from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (49 FR 46314). On November 9, 1984, the Administrator directed that Agency offices use the proposed guidelines in performing risk assessments until final guidelines become available.

After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and preliminary Agency responses to those comments. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for Mutagenicity Risk Assessment were concurred on in a letter dated September 24, 1985. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The Agency is continuing to study the risk assessment issues raised in the guidelines and will revise these Guidelines in line with new information as appropriate.

References, supporting documents, and comments received on the proposed guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management

[51 FR 34007]

and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

CONTENTS

Part A: Guidelines for Mutagenicity Risk Assessment

I. Introduction

This section describes the procedures that the U.S. Environmental Protection Agency will follow in evaluating the potential genetic risk associated with human exposure to chemicals. The central purpose of the health risk assessment is to provide a judgment concerning the weight of evidence that an agent is a potential human mutagen, capable of inducing transmitted genetic changes, and, if so, to provide a judgment on how great an impact this agent is likely to have on public health. Regulatory decision making involves two components: risk assessment and risk management. Risk assessment estimates the potential adverse health consequences of exposure to toxic chemicals; risk management combines the risk assessment with the directives of the enabling regulatory legislation--together with socioeconomic, technical, political, and other considerations--to reach a decision as to whether or how much to control future exposure to the chemicals. The issue of risk management will not be dealt with in these Guidelines.

Risk assessment is comprised of the following components: hazard identification, dose-response assessment, exposure assessment, and risk characterization (1). Hazard identification is the qualitative risk assessment, dealing with the inherent toxicity of a chemical substance. The qualitative mutagenicity assessment answers the question of how likely an agent is to be a human mutagen. The three remaining components

comprise quantitative risk assessment, which provides a numerical estimate of the public health consequences of exposure to an agent. The quantitative mutagenicity risk assessment deals with the question of how much mutational damage is likely to be produced by exposure to a given agent under particular exposure scenarios.

In a dose-response assessment, the relationship between the dose of a chemical and the probability of induction of an adverse effect is defined. The component generally entails an extrapolation from the high doses administered to experimental animals or noted in some epidemiologic studies to the low exposure levels expected from human contact with the chemical in the environment.

The exposure assessment identifies populations exposed to toxic chemicals, describes their composition and size, and presents the types, magnitudes, frequencies, and durations of exposure to the chemicals. This component is developed independently of the other components of the mutagenicity assessment and is addressed in separate Agency guidelines (2).

In risk characterization, the outputs of the exposure assessment and the dose-response assessment are combined to estimate quantitatively the mutation risk, which is expressed as either estimated increase of genetic disease per generation or per lifetime, or the fractional increase in the assumed background mutation rate of humans. In each step of the assessment, the strengths and weaknesses of the major assumptions need to be presented, and the nature and magnitude of uncertainties need to be characterized.

The procedures set forth in these Guidelines will ensure consistency in the Agency's scientific risk assessments for mutagenic effects. The necessity for a consistent approach to the evaluation of mutagenic risk from chemical substances arises from the authority conferred upon the Agency by a number of statutes to regulate potential mutagens. As appropriate, these Guidelines will apply to statutes administered by the Agency, including the Federal Insecticide, Fungicide, and Rodenticide Act; the Toxic Substances Control Act; the Clean Air Act; the Federal Water Pollution Control Act; the Safe Drinking Water Act; the Resource Conservation and Recovery Act; and the Comprehensive Environmental Response, Compensation, and Liability Act. Because each statute is administered by separate offices, a consistent Agency-wide approach for performing risk assessments is desirable.

The mutagenicity risk assessments prepared pursuant to these Guidelines will be utilized with the requirements and constraints of the applicable statutes to arrive at regulatory decisions concerning mutagenicity. The standards of the applicable statutes and regulations may dictate that additional considerations (e.g., the economic and social benefits associated with use of the chemical substance) will come into play in reaching appropriate regulatory decisions.

The Agency has not attempted to provide in the Guidelines a detailed discussion of the mechanisms of mutagenicity or of the various test systems that are currently in use to detect mutagenic potential. Background information on mutagenesis and mutagenicity test systems is available in "Identifying and Estimating the Genetic Impact of Chemical Mutagens", National Academy of Sciences (NAS) Committee on Chemical Environmental Mutagens (3), as well as in other recent publications (4, 5).

The Agency is concerned with the risk associated with both germ-cell mutations and somatic-cell mutations. Mutations carried in germ cells may be inherited by future generations and may contribute to genetic disease, whereas mutations occurring in somatic cells may be implicated in the etiology of several disease states, including cancer. These Guidelines, however, are only concerned with genetic damage as it relates to germ-cell mutations. The use of mutagenicity test results in the assessment of carcinogenic risk is described in the Guidelines for Carcinogen Risk Assessment (6).

As a result of the progress in the control of infectious diseases, increases in average human life span, and better procedures for identifying genetic disorders, a considerable heritable genetic disease burden has been recognized in the human population. It is estimated that at least 10% of all human disease is related to specific genetic abnormalities, such as abnormal composition, arrangement, or dosage of genes and chromosomes (3, 7, 8). Such genetic abnormalities can lead to structural or functional health impairments. These conditions may be expressed in *utero*; at the time of birth; or during infancy, childhood, adolescence, or adult life; they may be chronic or acute in nature. As a result, they often have a severe impact upon the affected individuals and their families in terms of physical and mental

[51 FR 34008]

suffering and economic losses, and upon society in general, which often becomes responsible for institutional care of severely affected individuals. Some examples of genetic disorders are Down and Klinefelter syndromes, cystic fibrosis, hemophilia, sickle-cell anemia, and achondroplastic dwarfism. Other commonly recognized conditions that are likely to have a genetic component include hypercholesterolemia, hypertension, pyloric stenosis, glaucoma, allergies, several types of cancer, and mental retardation. These disorders are only a few of the thousands that are at least partially genetically determined (9).

Estimation of the fraction of human genetic disorders that result from new mutations is difficult, although in certain specific cases insights are available (10). It is clear that recurring mutation is important in determining the incidence of certain genetic disorders, such as some chromosomal aberration syndromes (e.g., Down syndrome) and rare dominant and X-linked recessive diseases (e.g., achondroplasia and hemophilia A). For other single-factor disorders (e.g., sickle-cell anemia) and certain multifactorial disorders (e.g., pyloric stenosis), the contribution of new mutations to disease frequency is probably small. However, it is generally recognized that most newly-arising mutations that are phenotypically expressed are in some ways deleterious to the organism receiving them (3, 7, 8). Adverse effects may be manifested at the biochemical, cellular, or physiological levels of organization. Although mutations are the building blocks for further evolutionary change of species, it is believed that increases in the mutation rate could lead to an increased frequency of expressed genetic disorders in the first and subsequent generations.

Life in our technological society results in exposure to many natural and synthetic chemicals. Some have been shown to have mutagenic activity in mammalian and submammalian test systems, and thus may have the potential to increase genetic damage in the human population. Chemicals exhibiting mutagenic activity in various test systems have been found distributed among foods, tobacco, drugs, food additives, cosmetics, industrial compounds, pesticides, and consumer products. The extent to which exposure to natural and synthetic environmental agents may have increased the frequency of genetic disorders in the present human population and contributed to the mutational "load" that will be transmitted to future generations is unknown at this time. However, for the reasons cited above, it seems prudent to limit exposures to potential human mutagens.

A. Concepts Relating to Heritable Mutagenic Risk

These Guidelines are concerned with chemical substances or mixtures of substances that can induce alterations in the genome of either somatic or germinal cells. The mutagenicity of physical agents (e.g., radiation) is not addressed here. There are several mutagenic end points of concern to the Agency. These include point mutations (i.e., submicroscopic changes in the base sequence of DNA) and structural or numerical chromosome aberrations. Structural aberrations include deficiencies, duplications, insertions, inversions, and translocations, whereas numerical aberrations are gains or losses of whole chromosomes (e.g., trisomy, monosomy) or sets of chromosomes (haploidy, polyploidy).

Certain mutagens, such as alkylating agents, can directly induce alterations in the DNA. Mutagenic effects may also come about through mechanisms other than chemical alterations of DNA. Among these are interference with normal DNA synthesis (as caused by some metal mutagens), interference with DNA repair, abnormal DNA methylation, abnormal nuclear division processes, or lesions in non-DNA targets (e.g., protamine, tubulin).

Evidence that an agent induces heritable mutations in human beings could be derived from epidemiologic data indicating a strong association between chemical exposure and heritable effects. It is difficult to obtain such data because any specific mutation is a rare event, and only a small fraction of the estimated thousands of human genes and conditions are currently useful as markers in estimating mutation rates. Human genetic variability, small numbers of offspring per individual, and long generation times further complicate such studies. In addition, only disorders caused by dominant mutations, some sex-linked recessive mutations, and certain chromosome aberrations can be detected in the first generation after their occurrence. Conditions caused by autosomal recessive disorders (which appear to occur more frequently than dominant disorders) or by polygenic traits may go unrecognized for many generations. Therefore, in the absence of human epidemiological data, it is appropriate to rely on data from experimental animal systems as long as the limitations of using surrogate and model systems are clearly stated.

Despite species differences in metabolism, DNA repair, and other physiological processes affecting chemical mutagenesis, the virtual universality of DNA as the genetic material and of the genetic code provides a rationale for using various nonhuman test systems to predict the intrinsic mutagenicity of test chemicals. Additional support for the use of nonhuman systems is provided by the observation that chemicals causing genetic effects in one species or test system frequently cause similar effects in other species or systems. Evidence also exists that chemicals can induce genetic damage in somatic cells of exposed humans. For example, high doses of mutagenic chemotherapeutic agents have been shown to cause chromosomal abnormalities (11), sister chromatic exchange (11), and, quite probably, point mutations in human lymphocytes exposed *in vivo* (12). While these results are not in germ cells, they do indicate that it is possible to induce mutagenic events in human cells *in vivo*. Furthermore, a wide variety of different types of mutations have been observed in humans including numerical chromosome aberrations, translocations, base-pair substitutions, and frameshift mutations. Although the cause of these mutations is uncertain, it is clear from these observations that the human germ-cell DNA is subject to the same types of

mutational events that are observed in other species and test systems.

Certain test systems offer notable advantages: cost; anatomical, histological, and/or metabolic similarities to humans; suitability for handling large numbers of test organisms; a large data base; or a basis for characterizing genetic events.

B. Test Systems

Many test systems are currently available that can contribute information about the mutagenic potential of a test compound with respect to various genetic end points. These tests have recently been evaluated through the EPA Gene-Tox Programs and the results of Phase I have been published (5). The Agency's Office of Pesticides and Toxic Substances has published various testing guidelines for the detection of mutagenic effects (13, 14).

Test systems for detecting point mutations include those in bacteria, eukaryotic microorganisms, higher plants, insects, mammalian somatic cells in culture, and germinal cells of intact mammals. Data from heritable, mammalian germ-cell tests provide the best experimental evidence that a

[51 FR 34009]

chemical is a potential human germ-cell mutagen since these tests require that mutations occur in germinal cells and that they are transmitted to the next generation. To date, the most extensively used test for the induction of heritable mutation is the mouse specific-locus test which measures the induction of recessive mutations at seven loci concerned with coat color and ear morphology. While this test has a large data base compared to other germ-cell assays, it is difficult to extrapolate results to humans since recessive mutations may occur more frequently than dominants, and the impact of recessive mutations is not seen for many generations. Information on frequencies of induced mutations resulting in health disorders in the first generation may be obtained from mouse systems designed to detect skeletal abnormalities, cataracts, or general morphological abnormalities. However, these assays have been used to a relatively limited extent, and there is a need for additional studies with known, chemical germ-cell mutagens to further characterize the test systems. Because large numbers of offspring must usually be generated in the systems described above, it is not expected that many chemicals will be tested using these systems. To obtain data on a large number of environmental chemicals, it will be necessary to rely on other tests to identify and characterize hazards from gene mutations.

Test systems for detecting structural chromosome aberrations have been developed in a variety of organisms including higher plants, insects, fish, birds, and several mammalian species. Many of these assays can be performed *in vitro* or *in vivo*, and in either germ or somatic cells. Procedures available for detecting structural chromosome aberrations in mammalian germ cells include measurement of heritable translocations or dominant lethality, as well as direct cytogenetic analyses of germ cells and early embryos in rodents.

Some chemicals may cause numerical chromosome changes (i.e., aneuploidy) as their sole mutagenic effect. These agents may not be detected as mutagens if evaluated only in tests for DNA damage, gene mutations, or chromosome breakage and rearrangement. Therefore, it is important to consider tests for changes in chromosome number in the total assessment of mutagenic hazards. Although tests for the detection of variation in the chromosome number are still at an early stage of development, systems exist in such diverse organisms as fungi, Drosophila, mammalian cells in culture, and intact mammals (e.g., mouse X-chromosome loss assay). Aneuploidy can arise from disturbances in a number of events affecting the meiotic process (15, 16). Although the mechanisms by which nondisjunction occurs are not well understood, mitotic structures other than DNA may be the target molecules for at least some mechanisms of induced nondisjunction.

Other end points that provide information bearing on the mutagenicity of a chemical can be detected by a variety of test systems. Such tests measure DNA damage in eukaryotic or prokaryotic cells, unscheduled DNA synthesis in mammalian somatic and germ cells, mitotic recombination and gene conversion in yeast, and sister-chromatid exchange in mammalian somatic and germ cells. Results in these assays are useful because the induction of these end points often correlates positively with the potential of a chemical to induce mutations.

In general, for all three end points (i.e., point mutations and numerical and structural aberrations), the Agency will place greater weight on tests conducted in germ cells than in somatic cells, on tests performed *in vivo* rather than *in vitro*, in eukaryotes rather than prokaryotes, and in mammalian species rather than in submammalian species. Formal numerical weighting systems have been developed (17); however, the Agency has concluded that these do not readily accommodate such variables as dose range, route of exposure, and magnitude of response.

The Agency anticipates that from time to time somatic cell data from chemically exposed human beings will be available (e.g., cytogenetic markers in peripheral lymphocytes). When possible, the Agency will use such data in conjunction with somatic and germ cell comparisons from *in vivo* mammalian experimental systems as a component in performing risk assessments.

The test systems mentioned previously are not the only ones that will provide evidence of mutagenicity or related DNA effects. These systems are enumerated merely to demonstrate the breadth of the available techniques for characterizing mutagenic hazards, and to indicate the types of data that the Agency will consider in its evaluation of mutagenic potential of a chemical agent. Most systems possess certain limitations that must be taken into account. The selection and performance of appropriate tests for evaluating the risks associated with human exposure to any suspected mutagen will depend on sound scientific judgment and experience, and may necessitate consultation with geneticists familiar with the sensitivity and experimental design of the test system in question. In view of the rapid advances in test methodology, the Agency expects that both the number and quality of the tools for assessing genetic risk to human beings will increase with time. The Agency will closely monitor developments in mutagenicity evaluation and will refine its risk assessment scheme as better test systems become available.

II. Qualitative Assessment (Hazard Identification)

The assessment of potential human germ-cell mutagenic risk is a multistep process. The first step is an analysis of the evidence bearing on a chemical's ability to induce mutagenic events, while the second step involves an analysis of its ability to produce these events in the mammalian gonad. All relevant information is then integrated into a weight-of-evidence scheme which presents the strength of the information bearing on the chemical's potential ability to produce mutations in human germ cells. For chemicals demonstrating this potential, one may decide to proceed with an evaluation of the quantitative consequences of mutation following expected human exposure.

For hazard identification, it is clearly desirable to have data from mammalian germ-cell tests, such as the mouse specific-locus test for point mutations and the heritable translocation or germ-cell cytogenetic tests for structural chromosome aberrations. It is recognized, however, that in most instances such data will not be available, and alternative means of evaluation will be required. In such cases the Agency will evaluate the evidence bearing on the agent's mutagenic activity and the agent's ability to interact with or affect the mammalian gonadal target. When evidence exists that an agent possesses both these attributes, it is reasonable to deduce that the agent is a potential human germ-cell mutagen.

While mammalian germ-cell assays are presently primarily performed on male animals, a chemical cannot be considered to be a non-mutagen for mammalian germ cells unless it is shown to be negative in both sexes. Furthermore, because most mammalian germ-cell assays are performed in mice, it is noteworthy that the data from ionizing radiation suggest that the female mouse immature oocyte may not be an appropriate surrogate for the same stage in the human female in mutagenicity testing. However,

[51 FR 34010]

mutagenicity data on the maturing and mature oocyte of the mouse may provide a useful model for human risk assessment.

A. Mutagenic Activity

In evaluating chemicals for mutagenic activity, a number of factors will be considered: 1) genetic end points (e.g., gene mutations, structural or numerical chromosomal aberrations) detected by the test systems, 2) sensitivity and predictive value of the test systems for various classes of chemical compounds, 3) number of different test systems used for detecting each genetic end point, 4) consistency of the results obtained in different test systems and different species, 5) aspects of the dose-response relationship, and 6) whether the tests are conducted in accordance with appropriate test protocols agreed upon by experts in the field.

B. Chemical Interactions in the Mammalian Gonad

Evidence for chemical interaction in the mammalian gonad spans a range of different types of findings. Each chemical under consideration needs to be extensively reviewed since this type of evidence may be part of testing exclusive of mutagenicity per se (e.g., reproduction, metabolism, and mechanistic investigations). Although it is not possible to classify clearly each type of information that may be available on a chemical, two possible groups are illustrated.

1. *Sufficient evidence* of chemical interaction is given by the demonstration that an agent interacts with germ-cell DNA or other chromatin constituents, or that it induces such end points as unscheduled DNA synthesis, sister-chromatid exchange, or chromosomal aberrations in germinal cells.

2. *Suggestive evidence* will include the finding of adverse gonadal effects such as sperm abnormalities following acute, subchronic, or chronic toxicity testing, or findings of adverse reproductive effects such as decreased fertility, which are consistent with the chemical's interaction with germ cells.

C. Weight-of-Evidence Determination

The evidence for a chemical's ability to produce mutations and to interact with the germinal target are integrated into a weight-of-evidence judgment that the agent may pose a hazard as a potential human germ-cell mutagen. All information bearing on the subject, whether indicative of potential concern or not, must be evaluated. Whatever

evidence may exist from humans must also be factored into the assessment.

All germ-cell stages are important in evaluating chemicals because some chemicals have been shown to be positive in postgonial stages but not in gonia (18). When human exposures occur, effects on postgonial stages should be weighted by the relative sensitivity and the duration of the stages. Chemicals may show positive effects for some end points and in some test systems, but negative responses in others. Each review must take into account the limitations in the testing and in the types of responses that may exist.

To provide guidance as to the categorization of the weight of evidence, a classification scheme is presented to illustrate, in a simplified sense, the strength of the information bearing on the potential for human germ-cell mutagenicity. It is not possible to illustrate all potential combinations of evidence, and considerable judgment must be exercised in reaching conclusions. In addition, certain responses in tests that do not measure direct mutagenic end points (e.g., SCE induction in mammalian germ cells) may provide a basis for raising the weight of evidence from one category to another. The categories are presented in decreasing order of strength of evidence.

1. Positive data derived from human germ-cell mutagenicity studies, when available, will constitute the highest level of evidence for human mutagenicity.

2. Valid positive results from studies on heritable mutational events (of any kind) in mammalian germ cells.

3. Valid positive results from mammalian germ-cell chromosome aberration studies that do not include an intergeneration test.

4. Sufficient evidence for a chemical's interaction with mammalian germ cells, together with valid positive mutagenicity test results from two assay systems, at least one of which is mammalian (*in vitro* or *in vivo*). The positive results may both be for gene mutations or both for chromosome aberrations; if one is for gene mutations and the other for chromosome aberrations, both must be from mammalian systems.

5. Suggestive evidence for a chemical's interaction with mammalian germ cells, together with valid positive mutagenicity evidence from two assay systems as described under 4, above. Alternatively, positive mutagenicity evidence of less strength than defined under 4, above, when combined with sufficient evidence for a chemical's interaction with mammalian germ cells.

6. Positive mutagenicity test results of less strength than defined under 4, combined with suggestive evidence for a chemical's interaction with mammalian germ cells.

7. Although definitive proof of non-mutagenicity is not possible, a chemical could be classified operationally as a non-mutagen for human germ cells, if it gives valid negative test results for all end points of concern.

8. Inadequate evidence bearing on either mutagenicity or chemical interaction with mammalian germ cells.

III. Quantitative Assessment

The preceding section addressed primarily the processes of hazard identification, i.e., the determination of whether a substance is a potential germ-cell mutagen. Often, no further data will be available, and judgments will need to be based mainly on qualitative criteria. Quantitative risk assessment is a two-step process: determination of the heritable effect per unit of exposure (dose-response) and the relationship between mutation rate and disease incidence. The procedures that are presently accepted for the estimation of an increase in disease resulting from increased mutation have been described (3, 7, 8). Dose-response information is combined with anticipated levels and patterns of human exposure in order to derive a quantitative assessment (risk characterization).

A. Dose Response

Dose-response assessments can presently only be performed using data from *in vivo*, heritable mammalian germ-cell tests, until such time as other approaches can be demonstrated to have equivalent predictability. The morphological specific-locus and biochemical specific-locus assays can provide data on the frequencies of recessive mutations induced by different chemical exposure levels, and similar data can be obtained for heritable chromosomal damage using the heritable translocation test. Data on the frequencies of induced mutations resulting in health disorders in the first generation may be obtained from mouse systems designed to detect skeletal abnormalities, cataracts, or general morphological abnormalities. Assays that directly detect heritable health effects in the first generation may provide the best basis for predicting human health risks that result from mutagen exposure. The experimental data on induced mutation frequency are usually obtained at exposure levels much higher than those that will be experienced by human beings. An assessment of human risk is obtained by extrapolating the induced mutation frequency or the observed phenotypic

[51 FR 34011]

effect downward to the approximate level of anticipated human exposure. In performing these extrapolations, the Agency will place greater weight on data derived from exposures and exposure rates that most closely simulate those experienced by the human population under study.

The Agency will strive to use the most appropriate extrapolation models for risk analysis

and will be guided by the available data and mechanistic considerations in this selection. However, it is anticipated that for tests involving germ cells of whole mammals, few dose points will be available to define dose-response functions. The Agency is aware that for at least one chemical that has been tested for mutations in mammalian germ cells, there exist departures from linearity at low exposure and exposure rates in a fashion similar to that seen for ionizing radiation that has a low linear energy transfer (19). The Agency will consider all relevant models for gene and chromosomal mutations in performing low-dose extrapolations and will choose the most appropriate model. This choice will be consistent both with the experimental data available and with current knowledge of relevant mutational mechanisms.

An experimental approach for quantitative assessment of genetic risk, which may have utility in the future, uses molecular dosimetry data from intact mammals in conjunction with mutagenicity and dosimetry data from other validated test systems (20). The intact mammal is used primarily for relating the exposure level for a given route of administration of a chemical to germ-cell dose, i.e., the level of mutagen-DNA interactions. This information is then used in conjunction with results obtained from mutagenicity test systems in which the relationship between the induction of mutations and chemical interactions with DNA can be derived. With mutagen-DNA interactions as the common denominator, a relationship can be constructed between mammalian exposure and the induced mutation frequency. The amount of DNA binding induced by a particular chemical agent may often be determined at levels of anticipated human exposure.

For some mutagenic events, DNA may not necessarily be the critical target. Interaction of chemicals with other macromolecules, such as tubulin, which is involved in the separation of chromosomes during nuclear division, can lead to chromosomal nondisjunction. At present, general approaches are not available for dose-response assessments for these types of mutations. Ongoing research should provide the means to make future assessments on chemicals causing aneuploidy.

B. Exposure Asssessment

The exposure assessment identifies populations exposed to toxic chemicals; describes their composition and size; and presents the types, magnitudes, frequencies, and durations of exposure to the chemicals. This component is developed independently of the other components of the mutagenicity assessment (2).

C. Risk Characterization

In performing mutagenicity risk assessments, it is important to consider each genetic end point individually. For example, although certain chemical substances that interact with DNA may cause both point and chromosomal mutations, it is expected that the ratio of these events may differ among chemicals and between doses for a given chemical. Furthermore, transmissible chromosomal aberrations are recoverable with higher frequencies from meiotic and postmeiotic germ-cell stages, which have a brief life span, than in spermatogonial stem cells, which can accumulate genetic damage throughout the reproductive life of an individual. For these reasons, when data are available, the Agency, to the best extent possible, will assess risks associated with all genetic end points.

Any risk assessment should clearly delineate the strengths and weaknesses of the data, the assumptions made, the uncertainties in the methodology, and the rationale used in reaching the conclusions, e.g., similar or different routes of exposure and metabolic differences between humans and test animals. When possible, quantitative risk assessments should be expressed in terms of the estimated increase of genetic disease per generation, or the fractional increase in the assumed background spontaneous mutation rate of humans (7). Examples of quantitative risk estimates have been published (7, 8, 21); these examples may be of use in performing quantitative risk assessments for mutagens.

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[51 FR 34012]

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Part B: Response to Public and Science Advisory Board Comments

This section summarizes some of the issues raised in public and Science Advisory Board (SAB) comments on the Proposed Guidelines for Mutagenicity Risk Assessment published on November 23, 1984 (49 FR 46314). Unlike the other guidelines published on the same date, the Proposed Guidelines for Mutagenicity Risk Assessment contained a detailed section dealing with public comments received in response to the original proposal of 1980 (45 FR 74984). Several of the comments received in response to the proposed guidelines of 1984 were similar to those received in response to the proposed guidelines of 1980. Those comments are not addressed here because the position of the Agency on those issues has been presented in the responses included with the 1984 proposed guidelines (49 FR 46315- 46316).

A total of 44 comments were received in response to the proposed guidelines of 1984: 21 from manufacturers of regulated products, 10 from associations, 9 from government agencies, 2 from educational institutions, 1 from an individual, and 1 from a private consulting firm. The proposed guidelines and the public comments received were transmitted to the Agency's SAB prior to its public review of the proposed guidelines held April 22-23, 1985. The majority of the comments were favorable and expressed the opinion that the proposed guidelines accurately represent the existing state of knowledge in the field of mutagenesis. Several commentors offered suggestions for further clarification of particular issues, and many of the suggestions have been incorporated.

The two areas that received the most substantive comments were the sections concerning Weight-of-Evidence Determination and Dose Response. The comments on the proposed weight-of-evidence scheme ranged from suggestions for the elimination of a formal scheme to the expansion of the scheme to cover more potential data configurations. The SAB recommended an eight-level rank ordering scheme to define levels of evidence relating to human germ-cell mutagenicity. The Agency has incorporated this scheme into the Guidelines. Some commentors and the SAB suggested that the molecular dosimetry approach to dose-response data be presented as a concept that may be useful in the future rather than being available for use now. The Agency agrees that the data base at the present time is too sparse to recommend a general application of this approach to a wide range of chemical classes, and the Guidelines have been changed to reflect this. It should be noted, however, that the Agency strongly supports the development of molecular dosimetry methodologies as they relate to both an understanding of dose-response relationships and to methods for studying human exposure. A number of comments suggesting clarifications and editorial changes have been incorporated and the references have been expanded.

51 FR 34014

GUIDELINES FOR THE HEALTH RISK ASSESSMENT OF CHEMICAL MIXTURES

SUMMARY: On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for the Health Risk Assessment of Chemical Mixtures.

The Guidelines for the Health Risk Assessment of Chemical Mixtures (hereafter "Guidelines") are intended to guide Agency analysis of information relating to health effects data on chemical mixtures in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for the Health Risk Assessment of Chemical Mixtures published January 9, 1985 (50 FR 1170).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

FOR FURTHER INFORMATION CONTACT:

Dr. Richard Hertzberg
Methods Evaluation and Development Staff
Environmental Criteria and Assessment Office
U.S. Environmental Protection Agency
26 W. St. Clair Street
Cincinnati, OH 45268
513-569-7582

SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process*. In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for the Health Risk Assessment of Chemical Mixtures

Work on the Guidelines for the Health Risk Assessment of Chemical Mixtures began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the fields of toxicology, pharmacokinetics, and statistics from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (50 FR 1170). On November 9, 1984, the Administrator directed that Agency offices use the

proposed guidelines in performing risk assessments until final guidelines become available. After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and preliminary Agency responses to those comments. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for the Health Risk Assessment of Chemical Mixtures were concurred on in a letter dated August 16, 1985. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The SAB requested that the Agency develop a technical support document for these Guidelines. The SAB identified the need for this type of document due to the limited knowledge on interactions of chemicals in biological systems. Because of this, the SAB commented that progress in improving risk assessment will be particularly dependent upon progress in the science of interactions.

Agency staff have begun preliminary work on the technical support document and expect it to be completed by early 1987. The Agency is continuing to study the risk assessment issues raised in the guidelines and will revise these Guidelines in line with new information as appropriate.

[51 FR 34015]

References, supporting documents, and comments received on the proposed guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

CONTENTS

Part A: Guidelines for the Health Risk Assessment of Chemical Mixtures

I. Introduction

The primary purpose of this document is to generate a consistent Agency approach for evaluating data on the chronic and subchronic effects of chemical mixtures. It is a procedural guide that emphasizes broad underlying principles of the various science disciplines (toxicology, pharmacology, statistics) necessary for assessing health risk from chemical mixture exposure. Approaches to be used with respect to the analysis and evaluation of the various data are also discussed.

It is not the intent of these Guidelines to regulate any social or economic aspects concerning risk of injury to human health or the environment caused by exposure to a chemical agent(s). All such action is addressed in specific statutes and federal legislation and is independent of these Guidelines.

While some potential environmental hazards involve significant exposure to only a single compound, most instances of environmental contamination involve concurrent or sequential exposures to a mixture of compounds that may induce similar or dissimilar effects over exposure periods ranging from short-term to lifetime. For the purposes of these Guidelines, mixtures will be defined as any combination of two or more chemical substances regardless of source or of spatial or temporal proximity. In some instances, the mixtures are highly complex consisting of scores of compounds that are generated simultaneously as by-products from a single source or process (e.g., coke oven emissions and diesel exhaust). In other cases, complex mixtures of related compounds are produced as commercial products (e.g., PCBs, gasoline and pesticide formulations) and eventually released to the environment. Another class of mixtures consists of compounds, often unrelated chemically or commercially, which are placed in the same area for disposal or storage, eventually come into contact with each other, and are released as a mixture to the environment. The quality and quantity of pertinent information available for risk assessment varies considerably for different mixtures. Occasionally, the chemical composition of a mixture is well characterized, levels of exposure to the population are known, and detailed toxicologic data on the mixture are available. Most frequently, not all components of the mixture are known, exposure data are uncertain, and toxicologic data on the known components of the mixture are limited. Nonetheless, the Agency may be required to take action because of the number of individuals at potential risk or because of the known toxicologic effects of these compounds that have been identified in the mixture.

The prediction of how specific mixtures of toxicants will interact must be based on an understanding of the mechanisms of such interactions. Most reviews and texts that discuss toxicant interactions attempt to discuss the biological or chemical bases of the interactions (e.g., Klaassen and Doull, 1980; Levine, 1973; Goldstein et al., 1974; NRC, 1980a; Veldstra, 1956; Withey, 1981). Although different authors use somewhat different classification schemes when discussing the ways in which toxicants interact, it generally is recognized that toxicant interactions may occur during any of the toxicologic processes that take place with a single compound: absorption, distribution, metabolism, excretion, and activity at the receptor site(s). Compounds may interact chemically, yielding a new toxic component or causing a change in the biological availability of the existing component. They may also interact by causing different effects at different receptor sites.

Because of the uncertainties inherent in predicting the magnitude and nature of toxicant interactions, the assessment of health risk from chemical mixtures must include a thorough discussion of all assumptions. No single approach is recommended in these Guidelines. Instead, guidance is given for the use of several approaches depending on the nature and quality of the data. Additional mathematical details are presented in section IV.

In addition to these Guidelines, a supplemental technical support document is being developed which will contain a thorough review of all available information on the toxicity of chemical mixtures and a discussion of research needs.

II. Proposed Approach

No single approach can be recommended to risk assessments for multiple chemical exposures. Nonetheless, general guidelines can be recommended depending on the type of mixture, the known toxic effects of its components, the availability of toxicity data on the mixture or similar mixtures,

[51 FR 34016]

the known or anticipated interactions among components of the mixture, and the quality of the exposure data. Given the complexity of this issue and the relative paucity of empirical data from which sound generalizations can be constructed, emphasis must be placed on flexibility, judgment, and a clear articulation of the assumptions and limitations in any risk assessment that is developed. The proposed approach is summarized in Table 1 and Figure 1 and is detailed below. An alphanumeric scheme for ranking the quality of the data used in the risk assessment is given in Table 2.

A. Data Available on the Mixture of Concern

For predicting the effects of subchronic or chronic exposure to mixtures, the preferred approach usually will be to use subchronic or chronic health effects data on the mixture of concern and adopt procedures similar to those used for single compounds, either systemic toxicants or carcinogens (see U.S. EPA, 1986a-1986c). The risk assessor must recognize, however, that dose-response models used for single compounds are often based on biological mechanisms of the toxicity of single compounds, and may not be as well justified when applied to the mixture as a whole. Such data are most likely to be available on highly complex mixtures, such as coke oven emissions or diesel exhaust, which are generated in large quantities and associated with or suspected of causing adverse health effects. Attention should also be given to the persistence of the mixture in the environment as well as to the variability of the mixture composition over time or from different sources of emissions. If the components of the mixture are known to partition into different environmental compartments or to degrade or transform at different rates in the environment, then those factors must also be taken into account, or the confidence in and applicability of the risk assessment is diminished.

TABLE 1.-- RISK ASSESSMENT APPROACH FOR CHEMICAL MIXTURES

1. Assess the quality of the data on interactions, health effects, and exposure (see Table 2).
   a. If adequate, proceed to Step 2.
   b. If inadequate, proceed to Step 14.

2. Health effects information is available on the chemical mixture of concern .
   a. If yes, proceed to Step 3.
   b. If no, proceed to Step 4.

3. Conduct risk assessment on the mixture of concern based on health effects data on the mixture. Use the same procedures as those for single compounds. Proceed to Step 7 (optional) and Step 12.

4. Health effects information is available on a mixture that is similar to the mixture of concern.
   a. If yes, proceed to Step 5.
   b. If no, proceed to Step 7.

5. Assess the similarity of the mixture on which health effects data are available to the mixture of concern, with emphasis on any differences in components or proportions of components, as well as the effects that such differences would have on biological activity.
   a. If sufficiently similar, proceed to Step 6.
   b. If not sufficiently similar, proceed to Step 7.

6. Conduct risk assessment on the mixture of concern based on health effects data on the similar mixture. Use the same procedures as those for single compounds. Proceed to Step 7 (optional) and Step 12.

7. Compile health effects and exposure information on the components of the mixture.

8. Derive appropriate indices of acceptable exposure and/or risk on the individual components in the mixture. Proceed to Step 9.

9. Assess data on interactions of components in the mixtures.
   a. If sufficient quantitative data are available on the interactions of two or more components in the mixture, proceed to Step 10.
   b. If sufficient quantitative data are not available, use whatever information is available to qualitatively indicate the nature of potential interactions. Proceed to Step 11.

10. Use an appropriate interaction model to combine risk assessments on compounds for which data are adequate, and use an additivity assumption for the remaining compounds. Proceed to Step 11 (optional) and Step 12.

11. Develop a risk assessment based on an additivity approach for all compounds in the mixture. Proceed to Step 12.

12. Compare risk assessments conducted in Steps 5, 8, and 9. Identify and justify the preferred assessment, and quantify uncertainty, if possible. Proceed to Step 13.

13. Develop an integrated summary of the qualitative and quantitative assessments with special emphasis on uncertainties and assumptions. Classify the overall quality of the risk assessment, as indicated in Table 2. Stop.

14. No risk assessment can be conducted because of inadequate data on interactions, health effects, or exposure. Qualitatively assess the nature of any potential hazard and detail the types of additional data necessary to support a risk assessment. Stop.

Note. -- Several decisions used here, especially those concerning adequacy of data and similarity between two mixtures, are not precisely characterized and will require considerable judgment. See text.

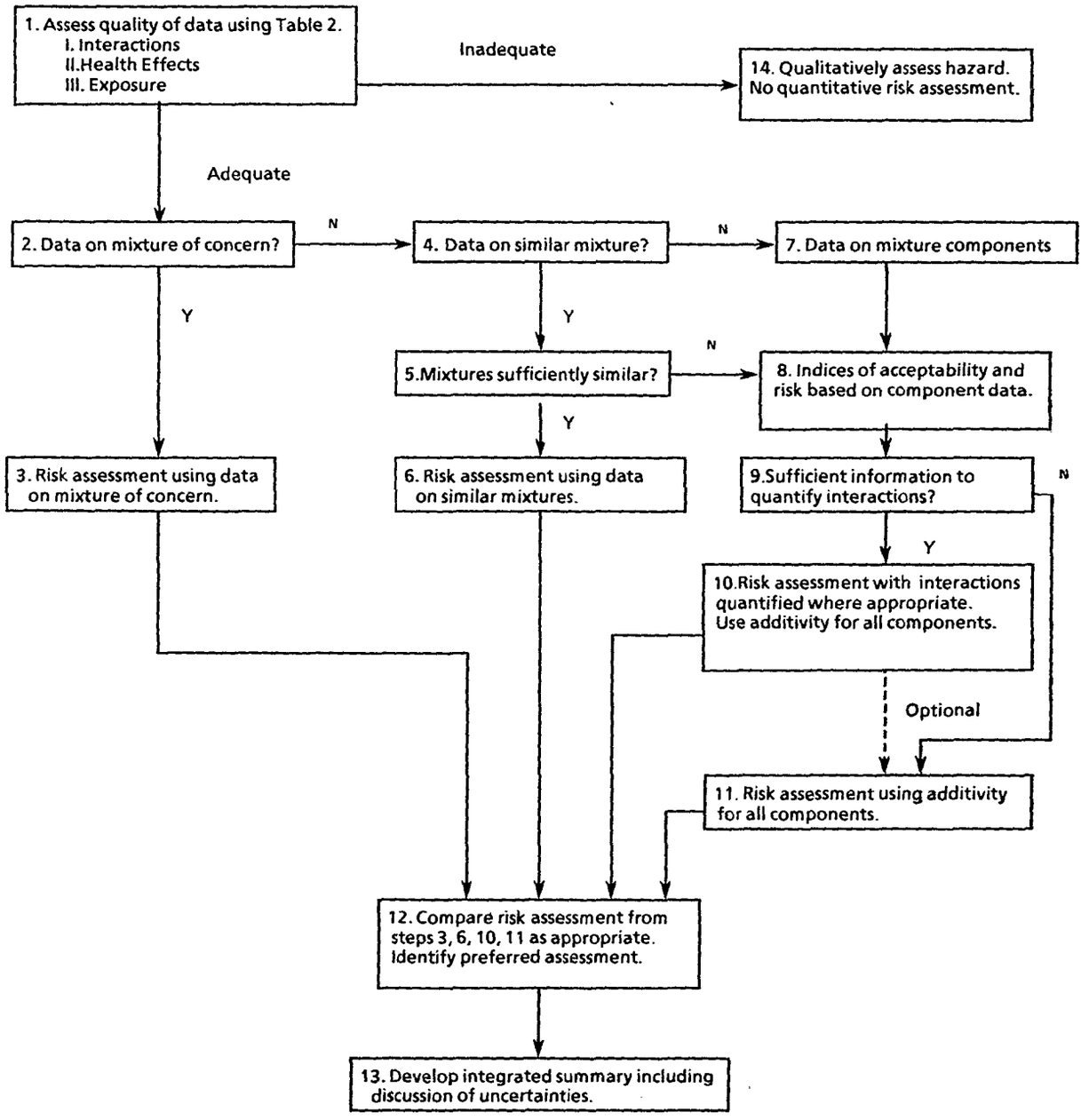

Figure 1. Flow chart of the risk assessment approach in Table 1. Note that it may be desirable to conduct all three assessments when possible (i.e., using data on the mixture, a similar mixture ,or the components) in order to make the fullest use of the available data. See text for further discussion.

TABLE 2. -- CLASSIFICATION SCHEME FOR THE QUALITY OF THE RISK ASSESSMENT OF THE MIXTURE[a]

Information on Interactions

I. Assessment is based on data on the mixture of concern.

II. Assessment is based on data on a sufficiently similar mixture.

III. Quantitative interactions of components are well characterized.

IV. The assumption of additivity is justified based on the nature of the health effects and on the number of component compounds.

V. An assumption of additivity cannot be justified, and no quantitative risk assessment can be conducted.

Health Effects Information

A. Full health effects data are available and relatively minor extrapolation is required.

B. Full health effects data are available but extensive extrapolation is required for route or duration of exposure or for species differences. These extrapolations are supported by pharmacokinetic considerations, empirical observations, or other relevant information.

C. Full health effects data are available, but extensive extrapolation is required for route or duration of exposure or for species differences. These extrapolations are not directly supported by the information available.

D. Certain important health effects data are lacking and extensive extrapolations are required for route or duration of exposure or for species differences.

E. A lack of health effects information on the mixture and its components in the mixture precludes a quantitative risk assessment.

Exposure Information[b]

1. Monitoring information either alone or in combination with modeling information is sufficient to accurately characterize human exposure to the mixture or its components.

2. Modeling information is sufficient to reasonably characterize human exposure to the mixture or its components.

3. Exposure estimates for some components are lacking, uncertain, or variable. Information on health effects or environmental chemistry suggest that this limitation is not likely to substantially affect the risk assessment.

4. Not all components in the mixture have been identified or levels of exposure are highly uncertain or variable. Information on health effects or environmental chemistry is not sufficient to assess the effect of this limitation on the risk assessment.

5. The available exposure information is insufficient for conducting a risk assessment.

B. Data Available on Similar Mixtures

If the risk assessment is based on data from a single mixture that is known to be generated with varying compositions depending on time or different emission sources, then the confidence in the applicability of the data to a risk assessment also is diminished. This can be offset to some degree if data are available on several mixtures of the same components that have different component ratios which encompass the temporal or spatial differences in composition of the mixture of concern. If such data are available, an attempt should be made to determine if significant and systematic differences exist among the chemical mixtures. If significant differences are noted, ranges of risk can be estimated based on the toxicologic data of the various mixtures. If no significant differences are noted, then a single risk assessment may be adequate, although the range of ratios of the components in the mixtures to which the risk assessment applies should also be given.

If no data are available on the mixtures of concern, but health effects data are available on a similar mixture (i.e., a mixture having the same components but in slightly different ratios, or having several common components but lacking one or more components, or having one or more additional components), a decision must be made whether the mixture on which health effects data are available is or is not "sufficiently similar" to the mixture of concern to permit a risk assessment. The determination of "sufficient similarity" must be made on a case-by-case basis, considering not only the uncertainties associated with using data on a dissimilar mixture but also the uncertainties of using other approaches such as additivity. In determining reasonable similarity, consideration should be given to any information on the components that differ or are contained in markedly different proportions between the mixture on which health effects data are available and the mixture of concern. Particular emphasis should be placed on any toxicologic or pharmacokinetic data on the components or the mixtures which would be useful in assessing the significance of any chemical difference between the similar mixture and the mixtures of concern.

Even if a risk assessment can be made using data on the mixtures of concern or a reasonably similar mixture, it may be desirable to conduct a risk assessment based on toxicity data on the

[a] See text for discussion of sufficient similarity, adequacy of data, and justification for additivity assumptions.

[b] See the Agency's Guidelines for Estimating Exposures (U.S. EPA, 1986d) for more complete information on performing exposure assessments and evaluating the quality of exposure data.

components in the mixture using the procedure outlined in section II.B. In the case of a mixture containing carcinogens and toxicants, an approach based on the mixture data alone may not be sufficiently protective in all cases. For example, this approach for a two-component mixture of one carcinogen and one toxicant would use toxicity data on the mixture of the two compounds. However, in a chronic study of such a mixture, the presence of the toxicant could mask the activity of the carcinogen. That is to say, at doses of the mixture sufficient to induce a carcinogenic effect, the toxicant could induce mortality so that at the maximum tolerated dose of the mixture, no carcinogenic effect could be observed. Since carcinogenicity is considered by the Agency to be a nonthreshold effect, it may not be prudent to construe the negative results of such a bioassay as indicating the absence of risk at lower doses. Consequently, the mixture approach should be modified to allow the risk assessor to evaluate the potential for masking, of one effect by another, on a case-by-case basis.

C. Data Available Only on Mixture Components

If data are not available on an identical or reasonably similar mixture, the risk assessment may be based on the toxic or carcinogenic properties of the components in the mixture. When little or no quantitative information is available on the potential interaction among the components, additive models (defined in the next section) are recommended for systemic toxicants. Several studies have demonstrated that dose additive models often predict reasonably well the toxicities of mixtures composed of a substantial variety of both similar and dissimilar compounds (Pozzani et al., 1959; Smyth et al., 1969, 1970; Murphy, 1980). The problem of multiple toxicant exposure has been addressed by the American Conference of Governmental Industrial Hygienists (ACGIH, 1983), the Occupational Safety and Health Administration (OSHA, 1983), the World Health Organization (WHO, 1981), and the National Research Council (NRC, 1980a, b). Although the focus and purpose of each group was somewhat different, all groups that recommended an approach elected to adopt some type of dose additive model. Nonetheless, as discussed in section IV, dose additive models are not the most biologically plausible approach if the compounds do not have the same mode of toxicologic action. Consequently, depending on the nature of the risk assessment and the available information on modes of action and patterns of joint action, the

most reasonable additive model should be used.

1. Systemic Toxicants. For systemic toxicants, the current risk assessment methodology used by the Agency for single compounds most often results in the derivation of an exposure level which is not anticipated to cause significant adverse effects. Depending on the route of exposure, media of concern, and the legislative mandate guiding the risk assessments, these exposure levels may be expressed in a variety of ways such as acceptable daily intakes (ADIs) or reference doses (RfDs), levels associated with various margins of safety (MOS), or acceptable concentrations in various media. For the purpose of this discussion, the term "acceptable level" (AL) will be used to indicate any such criteria or advisories derived by the Agency. Levels of exposure (E) will be estimates obtained following the most current Agency Guidelines for Estimating Exposures (U.S. EPA, 1986d). For such estimates, the "hazard index" (HI) of a mixture based on the assumption of dose addition may be defined as:

$$HI = E_1/AL_1 + E_2/AL_2 + \ldots + E_i/AL_i \qquad \text{(II-1)}$$

where:

E_i = exposure level to the i^{th} toxicant* and
AL_i = maximum acceptable level for the i^{th} toxicant.

Since the assumption of dose addition is most properly applied to compounds that induce the same effect by similar modes of action, a separate hazard index should be generated for each end point of concern. Dose addition for dissimilar effects does not have strong scientific support, and, if done, should be justified on a case-by-case basis in terms of biological plausibility.

The assumption of dose addition is most clearly justified when the mechanisms of action of the compounds under consideration are known to be the same. Since the mechanisms of action for most compounds are not well understood, the justification of the assumption of dose addition will often be limited to similarities in pharmacokinetic and toxicologic characteristics. In any event, if a hazard index is generated, the quality of the experimental evidence supporting the assumption of dose addition must be clearly articulated.

The hazard index provides a rough measure of likely toxicity and requires cautious interpretation. The hazard index is only a numerical indication of the nearness to acceptable limits of exposure or the degree to which acceptable exposure levels are exceeded. As this index approaches unity, concern for the potential hazard of the mixture increases. If the index exceeds unity, the concern is the same as if an individual chemical exposure exceeded its acceptable level by the same proportion. The hazard index does not define dose-response relationships, and its numerical value should not be construed to be a direct estimate of risk. Nonetheless, if sufficient data are available to derive individual acceptable levels for a spectrum of effects (e.g., MFO induction,

*See the Agency's guidelines (U.S. EPA, 1986d) for information on how to estimate this value.

variabilities of the acceptable levels are known, or if the acceptable levels are given as ranges (e.g., associated with different margins of safety), then the hazard index should be presented with corresponding estimates of variation or range. Most studies on systemic toxicity report only descriptions of the effects in each dose group. If dose-response curves are estimated for systemic toxicants, however, dose-additive or response-additive assumptions can be used, with preference given to the most biologically plausible assumption (see section IV for the mathematical details).

2. Carcinogens. For carcinogens, whenever linearity of the individual dose-response curves has been assumed (usually restricted to low doses), the increase in risk P (also called excess or incremental risk), caused by exposure d, is related to carcinogenic potency B, as:

$$P = d\,B \qquad \text{(II-2)}$$

For multiple compounds, this equation may be generalized to:

$$P = \Sigma d_i\,B_i \qquad \text{(II-3)}$$

This equation assumes independence of action by the several carcinogens and is equivalent to the assumption of dose addition as well as to response addition with completely negative correlation of tolerance, as long as $P < 1$ (see section IV). Analogous to the procedure used in equation II-1 for systemic toxicants, an index for n carcinogens can be developed by dividing exposure levels (E) by doses (DR) associated with a set level of risk:

$$HI = E_1/DR_1 + E_2/DR_2 + \ldots + E_n/DR_n \qquad \text{(II-4)}$$

Note that the less linear the dose-response curve is, the less appropriate equations II-3 and II-4 will be, perhaps even at low doses. It should be emphasized that because of the uncertainties in estimating dose-response relationships for single compounds, and the additional uncertainties in combining the individual estimate to assess response from exposure to mixtures, response rates and hazard indices may have merit in comparing risks but should not be regarded as measures of absolute risk.

3.Interactions. None of the above equations incorporates any form of synergistic or antagonistic interaction. Some types of information, however, may be available that suggest that two or more components in the mixture may interact. Such information must be assessed in terms of both its relevance to subchronic or chronic hazard and its suitability for quantitatively altering the risk assessment.

For example, if chronic or subchronic toxicity or carcinogenicity studies have been conducted that permit a quantitative estimation of interaction for two chemicals, then it may be desirable to consider using equations detailed in section IV, or modifications of these equations, to treat the two compounds as a single toxicant with greater or lesser potency than would be predicted from additivity. Other components of the mixture, on which no such interaction data are available, could then be separately treated in an additive manner. Before such a procedure is adopted, however, a discussion should be presented of the likelihood that other compounds in the mixture may interfere with the interaction of the two toxicants on which quantitative interaction data are available. If the weight of evidence suggests that interference is likely, then a quantitative alteration of the risk assessment may not be justified. In such cases, the risk assessment may only indicate the likely nature of interactions, either synergistic or antagonistic, and not quantify their magnitudes.

Other types of information, such as those relating to mechanisms of toxicant interaction, or quantitative estimates of interaction between two chemicals derived from acute studies, are even less likely to be of use in the quantitative assessment of long-term health risks. Usually it will be appropriate only to discuss these types of information, indicate the relevance of the information to subchronic or chronic exposure, and indicate, if possible, the nature of potential interactions, without attempting to quantify their magnitudes.

When the interactions are expected to have a minor influence on the mixture's toxicity, the assessment should indicate, when possible, the compounds most responsible for the predicted toxicity. This judgment should be based on predicted toxicity of each component,

[51 FR 34020]

based on exposure and toxic or carcinogenic potential. This potential alone should not be used as an indicator of the chemicals posing the most hazard.

4.Uncertainties. For each risk assessment, the uncertainties should be clearly discussed and the overall quality of the risk assessment should be characterized. The scheme outlined in Table 2 should be used to express the degree of confidence in the quality of the data on interaction, health effects, and exposure.

a. Health Effects--In some cases, when health effects data are incomplete, it may be possible to argue by analogy or quantitative structure-activity relationships that the compounds on which no health effects data are available are not likely to significantly affect the toxicity of the mixture. If a risk assessment includes such an argument, the limitations of the approach must be clearly articulated. Since a methodology has not been adopted for estimating an acceptable level (e.g., ADI) or carcinogenic potential for single compounds based either on quantitative structure-activity relationships or on the results of short-term screening tests, such methods are not at present

recommended as the sole basis of a risk assessment on chemical mixtures.

b. Exposure Uncertainties--The general uncertainties in exposure assessment have been addressed in the Agency's Guidelines for Estimating Exposures (U.S. EPA, 1986d). The risk assessor should discuss these exposure uncertainties in terms of the strength of the evidence used to quantify the exposure. When appropriate, the assessor should also compare monitoring and modeling data and discuss any inconsistencies as a source of uncertainty. For mixtures, these uncertainties may be increased as the number of compounds of concern increases.

If levels of exposure to certain compounds known to be in the mixture are not available, but information on health effects and environmental persistence and transport suggest that these compounds are not likely to be significant in affecting the toxicity of the mixture, then a risk assessment can be conducted based on the remaining compounds in the mixture, with appropriate caveats. If such an argument cannot be supported, no final risk assessment can be performed until adequate monitoring data are available. As an interim procedure, a risk assessment may be conducted for those components in the mixture for which adequate exposure and health effects data are available. If the interim risk assessment does not suggest a hazard, there is still concern about the risk from such a mixture because not all components in the mixture have been considered.

c. Uncertainties Regarding Composition of the Mixture--In perhaps a worst case scenario, information may be lacking not only on health effects and levels of exposure, but also on the identity of some components of the mixture. Analogous to the procedure described in the previous paragraph, an interim risk assessment can be conducted on those components of the mixture for which adequate health effects and exposure information are available. If the risk is considered unacceptable, a conservative approach is to present the quantitative estimates of risk, along with appropriate qualifications regarding the incompleteness of the data. If no hazard is indicated by this partial assessment, the risk assessment should not be quantified until better health effects and monitoring data are available to adequately characterize the mixture exposure and potential hazards.

III. Assumptions and Limitations

A. Information on Interactions

Most of the data available on toxicant interactions are derived from acute toxicity studies using experimental animals in which mixtures of two compounds were tested, often in only a single combination. Major areas of uncertainty with the use of such data involve the appropriateness of interaction data from an acute toxicity study for quantitatively altering a risk assessment for subchronic or chronic exposure, the appropriateness of interaction data on two component mixtures for quantitatively altering a risk assessment on a mixture of several compounds, and the accuracy of interaction data on experimental animals for quantitatively predicting interactions in humans.

The use of interaction data from acute toxicity studies to assess the potential interactions on chronic exposure is highly questionable unless the mechanism(s) of the interaction on acute exposure were known to apply to low-dose chronic exposure. Most known biological mechanisms for toxicant interactions, however, involve some form of competition between the chemicals or phenomena involving saturation of a receptor site or metabolic pathway. As the doses of the toxicants are decreased, it is likely that these mechanisms either no longer will exert a significant effect or will be decreased to an extent that cannot be measured or approximated.

The use of information from two-component mixtures to assess the interactions in a mixture containing more than two compounds also is questionable from a mechanistic perspective. For example, if two compounds are known to interact, either synergistically or antagonistically, because of the effects of one compound on the metabolism or excretion of the other, the addition of a third compound which either chemically alters or affects the absorption of one of the first two compounds could substantially alter the degree of the toxicologic interaction. Usually, detailed studies quantifying toxicant interactions are not available on multicomponent mixtures, and the few studies that are available on such mixtures (e.g., Gullino et al., 1956) do not provide sufficient information to assess the effects of interactive interference.

Concerns with the use of interaction data on experimental mammals to assess interactions in humans is based on the increasing appreciation for systematic differences among species in their response to individual chemicals. If systematic differences in toxic sensitivity to single chemicals exist among species, then it seems reasonable to suggest that the magnitude of toxicant interactions among species also may vary in a systematic manner. Consequently, even if excellent chronic data are available on the magnitude of toxicant interactions in a species of experimental mammal, there is uncertainty that the magnitude of the interaction will be the same in humans. Again, data are not available to properly assess the significance of this uncertainty.

Last, it should be emphasized that none of the models for toxicant interaction can predict the magnitude of toxicant interactions in the absence of extensive data. If sufficient data are available to

estimate interaction coefficients as described in section IV, then the magnitude of the toxicant interactions for various proportions of the same components can be predicted. The availability of an interaction ratio (observed response divided by predicted response) is useful only in assessing the magnitude of the toxicant interaction for the specific proportions of the mixture which was used to generate the interaction ratio.

The basic assumption in the recommended approach is that risk assessments on chemical mixtures are best conducted using toxicologic data on the mixture of concern or a reasonably similar mixture. While such risk

[51 FR 34021]

assessments do not formally consider toxicologic interactions as part of a mathematical model, it is assumed that responses in experimental mammals or human populations noted after exposure to the chemical mixture can be used to conduct risk assessments on human populations. In bioassays of chemical mixtures using experimental mammals, the same limitations inherent in species-to-species extrapolation for single compounds apply to mixtures. When using health effects data on chemical mixtures from studies on exposed human populations, the limitations of epidemiologic studies in the risk assessment of single compounds also apply to mixtures. Additional limitations may be involved when using health effects data on chemical mixtures if the components in the mixture are not constant or if the components partition in the environment.

B. Additivity Models

If sufficient data are not available on the effects of the chemical mixture of concern or a reasonably similar mixture, the proposed approach is to assume additivity. Dose additivity is based on the assumption that the components in the mixture have the same mode of action and elicit the same effects. This assumption will not hold true in most cases, at least for mixtures of systemic toxicants. For systemic toxicants, however, most single compound risk assessments will result in the derivation of acceptable levels, which, as currently defined, cannot be adapted to the different forms of response additivity as described in section IV.

Additivity models can be modified to incorporate quantitative data on toxicant interactions from subchronic or chronic studies using the models given in section IV or modifications of these models. If this approach is taken, however, it will be under the assumption that other components in the mixture do not interfere with the measured interaction. In practice, such subchronic or chronic interactions data seldom will be available. Consequently, most risk assessments (on mixtures) will be based on an assumption of additivity, as long as the components elicit similar effects.

Dose-additive and response-additive assumptions can lead to substantial errors in risk estimates if synergistic or antagonistic interactions occur. Although dose additivity has been shown to predict the acute toxicities of many mixtures of similar and dissimilar compounds (e.g., Pozzani et al., 1959; Smyth et al., 1969, 1970; Murphy, 1980), some marked exceptions have been noted. For example, Smyth et al. (1970) tested the interaction of 53 pairs of industrial chemicals based on acute lethality in rats. For most pairs of compounds, the ratio of the predicted LD_{50} to observed LD_{50} did not vary by more than a factor of 2. The greatest variation was seen with an equivolume mixture of morpholine and toluene, in which the observed LD_{50} was about five times less than the LD_{50} predicted by dose addition. In a study by Hammond et al. (1979), the relative risk of lung cancer attributable to smoking was 11, while the relative risk associated with asbestos exposure was 5. The relative risk of lung cancer from both smoking and asbestos exposure was 53, indicating a substantial synergistic effect. Consequently, in some cases, additivity assumptions may substantially underestimate risk. In other cases, risk may be overestimated. While this is certainly an unsatisfactory situation, the available data on mixtures are insufficient for estimating the magnitude of these errors. Based on current information, additivity assumptions are expected to yield generally neutral risk estimates (i.e., neither conservative nor lenient) and are plausible for component compounds that induce similar types of effects at the same sites of action.

IV. Mathematical Models and the Measurement of Joint Action

The simplest mathematical models for joint action assume no interaction in any mathematical sense. They describe either dose addition or response addition and are motivated by data on acute lethal effects of mixtures of two compounds.

A. Dose Addition

Dose addition assumes that the toxicants in a mixture behave as if they were dilutions or concentrations of each other, thus the true slopes of the dose-response curves for the individual compounds are identical, and the response elicited by the mixture can be predicted by summing the individual doses after adjusting for differences in potency; this is defined as the ratio of equitoxic doses. Probit transformation typically makes this ratio constant at all doses when parallel straight lines are obtained. Although this assumption can be applied to any model (e.g., the one-hit model in NRC, 1980b), it has been most often used in toxicology with the log-dose probit response model, which will be used to illustrate the assumption of dose addition.

Suppose that two toxicants show the following log-dose probit response equations:

$$Y_1 = 0.3 + 3 \log Z_1 \quad \text{(IV-1)}$$
$$Y_2 = 1.2 + 3 \log Z_2 \quad \text{(IV-2)}$$

where Y_i is the probit response associated with a dose of Z_i ($i = 1,2$). The potency, p, of toxicant #2 with respect to toxicant #1 is defined by the quantity Z_1/Z_2 when $Y_1 = Y_2$ (that is what is meant by equitoxic doses). In this example, the potency, p, is approximately 2. Dose addition assumes that the response, Y, to any mixture of these two toxicants can be predicted by:

$$Y = 0.3 + 3 \log (Z_1 + pZ2) \quad \text{(IV-3)}$$

Thus, since p is defined as Z_1/Z_2, equation IV-3 essentially converts Z_2 into an equivalent dose of Z by adjusting for the difference in potency. A more generalized form of this equation for any number of toxicants is:

$$Y = a_1 + b \log (f_1 + \Sigma f_i p_i) + b \log Z \quad \text{(IV-4)}$$

where:

a_1 = the y-intercept of the dose-response equation for toxicant #1
b = the slope of the dose-response lines for the toxicants
f_i = the proportion of the i^{th} toxicant in the mixture
p_i = the potency of the i^{th} toxicant with respect to toxicant #1 (i.e., Z_1/Z_i), and
Z = the sum of the individual doses in the mixture.

A more detailed discussion of the derivation of the equations for dose addition is presented by Finney (1971).

B. Response Addition

The other form of additivity is referred to as response addition. As detailed by Bliss (1939), this type of joint action assumes that the two toxicants act on different receptor systems and that the correlation of individual tolerances may range from completely negative ($r = -1$) to completely positive ($r = +1$). Response addition assumes that the response to a given concentration of a mixture of toxicants is completely determined by the responses to the components and the pairwise correlation coefficient. Taking P as the proportion of organisms responding to a mixture of two toxicants which evoke individual responses of P_1 and P_2, then

$P = P_1$ if $r = 1$ and $P_1 \geq P_2$ (IV-5)
$P = P_2$ if $r = 1$ and $P_1 < P_2$ (IV-6)
$P = P_1 + P_2 (1-P_1)$ if $r = 0$ (IV-7)
$P = P_1 + P_2$ if $r = -1$ and $P \leq 1$. (IV-8)

More generalized mathematical models for this form of joint action have been given by Plackett and Hewlett (1948).

C. Interactions

All of the above models assume no interactions and therefore do not incorporate measurements of synergistic or antagonistic effects. For measuring toxicant interactions for mixtures of two compounds, Finney (1942) proposed the

following modification of equation IV-4 for dose addition:

$$Y = a_1 + b \log (f_1 + pf_2 + K[pf_1f_2]^{0.5}) + b \log Z \quad \text{(IV-9)}$$

where a_1, b, f_1, f_2, p, and Z are defined as before, and K is the coefficient of interaction. A positive value of K indicates synergism, a negative value indicates antagonism, and a value of zero corresponds to dose addition as in equation IV-4. Like other proposed modifications of dose addition (Hewlett, 1969), the equation assumes a consistent interaction throughout the entire range of proportions of individual components. To account for such asymmetric patterns of interaction as those observed by Alstott et al. (1973), Durkin (1981) proposed the following modification to equation IV-9:

$$Y = a_1 + b \log (f_1 + pf_2 + K_1f_1[pf_1f_2]^{0.5} + K_2f_2[pf_1f_2]^{0.5}) + b \log Z \quad \text{(IV-10)}$$

in which $K(pf_1f_2)^{0.5}$ is divided into two components, $K_1f_1(pf_1f_2)^{0.5}$ and $K_2f_2(pf_1f_2)^{0.5}$. Since K_1 and K_2 need not have the same sign, apparent instances of antagonism at one receptor site and synergism at another receptor site can be estimated. When K_1 and K_2 are equal, equation IV-10 reduces to equation IV-9. It should be noted that to obtain a reasonable number of degrees of freedom in the estimation of K in equation IV-9 or K_1 and K_2 in equation IV-10, the toxicity of several different combinations of the two components must be assayed along with assays of the toxicity of the individual components. Since this requires experiments with large numbers of animals, such analyses have been restricted for the most part to data from acute bioassays using insects (e.g., Finney, 1971) or aquatic organisms (Durkin, 1979). Also, because of the complexity of experimental design and the need for large numbers of animals, neither equation IV-9 nor equation IV-10 has been generalized or applied to mixtures of more than two toxicants. Modifications of response-additive models to include interactive terms have also been proposed, along with appropriate statistical tests for the assumption of additivity (Korn and Liu, 1983; Wahrendorf et al., 1981).

In the epidemiologic literature, measurements of the extent of toxicant interactions, S, can be expressed as the ratio of observed relative risk to relative risk predicted by some form of additivity assumption. Analogous to the ratio of interaction in classical toxicology studies, $S = 1$ indicates no interaction, $S > 1$ indicates synergism, and $S < 1$ indicates antagonism. Several models for both

additive and multiplicative risks have been proposed (e.g., Hogan et al., 1978; NRC, 1980b; Walter, 1976). For instance, Rothman (1976) has discussed the use of the following measurement of toxicant interaction based on the assumption of risk additivity:

$$S = (R_{11} - 1)/(R_{10} + R_{01} - 2) \qquad \text{(IV-11)}$$

where R_{10} is the relative risk from compound #1 in the absence of compound #2, R_{01} is the relative risk from compound #2 in the absence of compound #1, and R_{11} is the relative risk from exposure to both compounds. A multiplicative risk model adapted from Walter and Holford (1978, equation 4) can be stated as:

$$S = R_{11}/(R_{10}R_{01}) \qquad \text{(IV-12)}$$

As discussed by both Walter and Holford (1978) and Rothman (1976), the risk-additive model is generally applied to agents causing diseases while the multiplicative model is more appropriate to agents that prevent disease. The relative merits of these and other indices have been the subject of considerable discussion in the epidemiologic literature (Hogan et al., 1978; Kupper and Hogan, 1978; Rothman, 1978; Rothman et al., 1980; Walter and Holford, 1978). There seems to be a consensus that for public health concerns regarding causative (toxic) agents, the additive model is more appropriate.

Both the additive and multiplicative models assume statistical independence in that the risk associated with exposure to both compounds in combination can be predicted by the risks associated with separate exposure to the individual compounds. As illustrated by Siemiatycki and Thomas (1981) for multistage carcinogenesis, the better fitting statistical model will depend not only upon actual biological interactions, but also upon the stages of the disease process which the compounds affect. Consequently, there is no *a priori* basis for selecting either type of model in a risk assessment. As discussed by Stara et al. (1983), the concepts of multistage carcinogenesis and the effects of promoters and cocarcinogens on risk are extremely complex issues. Although risk models for promoters have been proposed (e.g., Burns et al., 1983), no single approach can be recommended at this time.

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Part B: Response to Public and Science Advisory Board Comments

I. Introduction

This section summarizes some of the major issues raised in public comments on the Proposed Guidelines for the Health Risk Assessment of Chemical Mixtures published on January 9, 1985 (50 FR 1170). Comments were received from 14 individuals or organizations. An issue paper reflecting public and external review comments was presented to the Chemical Mixtures Guidelines Panel of the Science Advisory Board (SAB) on March 4, 1985. At its April 22-23, 1985, meeting, the SAB Panel provided the Agency with additional suggestions and recommendations concerning the Guidelines. This section also summarizes the issues raised by the SAB.

The SAB and public commentors expressed diverse opinions and addressed issues from a variety of perspectives. In response to comments, the Agency has modified or clarified many sections of the Guidelines, and is planning to develop a technical support document in line with the SAB recommendations. The discussion that follows highlights significant issues raised in the comments, and the Agency's response to them. Also, many minor recommendations, which do not warrant discussion here, were adopted by the Agency.

II. Recommended Procedures

A. Definitions

Several comments were received concerning the lack of definitions for certain key items and the general understandability of certain sections. Definitions have been rewritten for several terms and the text has been significantly rewritten to clarify the Agency's intent and meaning.

Several commentors noted the lack of a precise definition of "mixture," even though several classes of mixtures are discussed. In the field of chemistry, the term "mixture" is usually differentiated from true solutions, with the former defined as nonhomogeneous multicomponent systems. For these Guidelines, the term "mixture" is defined as "...any combination of two or more chemicals regardless of spatial or temporal homogeneity of source" (section 1). These Guidelines are intended to cover risk assessments for any situation where the population is exposed or potentially exposed to two or more compounds of concern. Consequently, the introduction has been revised to clarify the intended breadth of application.

Several commentors expressed concern that "sufficient similarity" was difficult to define and that the Guidelines should give more details concerning similar mixtures. The Agency agrees and is planning research projects to improve on the definition. Characteristics such as composition and toxic end-effects are certainly important, but the best indicators of similarity in terms of risk assessment have yet to be determined. The discussion in the Guidelines emphasizes case-by-case judgment until the necessary research can be performed. The Agency considered but rejected adding an example, because it is not likely that any single example would be adequate to illustrate the variety in the data and types of judgments that will be required in applying this concept. Inclusion of examples is being considered for the technical support document.

B. Mixtures of Carcinogens and Systemic Toxicants

The applicability of the preferred approach for a mixture of carcinogens and systemic (noncarcinogenic) toxicants was a concern of several public commentors as well as the SAB. The Agency realizes that the preferred approach of using test data on the mixture itself may not be sufficiently protective in all cases. For example, take a simple two-component mixture of one carcinogen and one toxicant. The preferred approach would lead to using toxicity data on the mixture of the two compounds. However, it is possible to set the proportions of each component so that in a chronic bioassay of such a mixture, the presence of the toxicant could mask the activity of the carcinogen. That is to say, at doses of

the mixture sufficient for the carcinogen to induce tumors in the small

[51 FR 34024]

experimental group, the toxicant could induce mortality. At a lower dose in the same study, no adverse effects would be observed, including no carcinogenic effects. The data would then suggest use of a threshold approach. Since carcinogenicity is considered by the Agency to be a nonthreshold effect, it may not be prudent to construe the negative results of such a bioassay as indicating the absence of risk at lower doses. Consequently, the Agency has revised the discussion of the preferred approach to allow the risk assessor to evaluate the potential for masking of carcinogenicity or other effects on a case-by-case basis. Another difficulty occurs with such a mixture when the risk assessment needs to be based on data for the mixture components. Carcinogens and systemic toxicants are evaluated by the Agency using different approaches and generally are described by different types of data: response rates for carcinogens vs. effect descriptions for toxicants. The Agency recognizes this difficulty and recommends research to develop a new assessment model for combining these dissimilar data sets into one risk estimate. One suggestion in the interim is to present separate risk estimates for the dissimilar end points, including carcinogenic, teratogenic, mutagenic, and systemic toxicant components.

III. Additivity Assumption

Numerous comments were received concerning the assumption of additivity, including:

a. the applicability of additivity to "complex" mixtures;
b. the use of dose additivity for compounds that induce different effects;
c. the interpretation of the Hazard Index; and
d. the use of interaction data.

Parts of the discussion in the proposed guidelines concerning the use of additivity assumptions were vague and have been revised in the final Guidelines to clarify the Agency's intent and position.

A. Complex Mixtures

The issue of the applicability of an assumption of additivity to complex mixtures containing tens or hundreds of components was raised in several of the public comments. The Agency and its reviewers agree that as the number of compounds in the mixture increases, an assumption of additivity will become less reliable in estimating risk. This is based on the fact that each component estimate of risk or an acceptable level is associated with some error and uncertainty. With current knowledge, the uncertainty will increase as the number of components increases. In any event, little experimental data are available to determine the general change in the error as the mixture contains more components. The Agency has decided that a limit to the number of components should not be set in these Guidelines. However, the Guidelines do explicitly state that as the number of compounds in the mixture increases, the uncertainty associated with the risk assessment is also likely to increase.

B. Dose Additivity

Commentors were concerned about what appeared to be a recommendation of the use of dose additivity for compounds that induce different effects. The discussion following the dose additivity equation was clarified to indicate that the act of combining all compounds, even if they induce dissimilar effects, is a screening procedure and not the preferred procedure in developing a hazard index. The Guidelines were further clarified to state that dose (or response) additivity is theoretically sound, and therefore best applied for assessing mixtures of similar acting components that do not interact.

C. Interpretation of the Hazard Index

Several comments addressed the potential for misinterpretation of the hazard index, and some questioned its validity, suggesting that it mixes science and value judgments by using "acceptable" levels in the calculation. The Agency agrees with the possible confusion regarding its use and has revised the Guidelines for clarification. The hazard index is an easily derived restatement of dose additivity, and is, therefore, most accurate when used with mixture components that have similar toxic action. When used with components of unknown or dissimilar action, the hazard index is less accurate and should be interpreted only as a rough indication of concern. As with dose addition, the uncertainty associated with the hazard index increases as the number of components increases, so that it is less appropriate for evaluating the toxicity of complex mixtures.

D. Use of Interaction Data

A few commentors suggested that any interaction data should be used to quantitatively alter the risk assessment. The Agency disagrees. The current information on interactions is meager, with only a few studies comparing response to the mixture with that predicted by studies on components. Additional uncertainties include exposure variations due to changes in composition, mixture dose, and species differences in the extent of the interaction. The Agency is constructing an interaction data base in an attempt to answer some of these issues. Other comments concerned the use of different types of interaction data. The Guidelines restrict the use of interaction data to that obtained from whole animal bioassays of a duration appropriate to the risk assessment. Since such data are frequently lacking, at least for chronic or subchronic effects, the issue is whether to allow for the use of other information such as acute data, *in*

vitro data, or structure-activity relationships to quantitatively alter the risk assessment, perhaps by use of a safety factor. The Agency believes that sufficient scientific support does not exist for the use of such data in any but a qualitative discussion of possible synergistic or antagonistic effects.

IV. Uncertainties and the Sufficiency of the Data Base

In the last two paragraphs of section II of the Guidelines, situations are discussed in which the risk assessor is presented with incomplete toxicity, monitoring, or exposure data. The SAB, as well as several public commentors, recommended that the "risk management" tone of this section be modified and that the option of the risk assessor to decline to conduct a risk assessment be made more explicit.

This is a difficult issue that must consider not only the quality of the available data for risk assessment, but also the needs of the Agency in risk management. Given the types of poor data often available, the risk assessor may indicate that the risk assessment is based on limited information and thus contains no quantification of risk. Nonetheless, in any risk assessment, substantial uncertainties exist. It is the obligation of the risk assessor to provide an assessment, but also to ensure that all the assumptions and uncertainties are articulated clearly and quantified whenever possible.

The SAB articulated several other recommendations related to uncertainties, all of which have been followed in the revision of the Guidelines. One recommendation was that the summary procedure table also be presented as a flow chart so that all options are clearly displayed. The SAB further recommended the development of a system to express the level of confidence in the various steps of the risk assessment.

The Agency has revised the summary table to present four major options: risk assessment using data on the mixture

[51 FR 34025]

itself, data on a similar mixture, data on the mixture's components, or declining to quantify the risk when the data are inadequate. A flow chart of this table has also been added to more clearly depict the various options and to suggest the combining of the several options to indicate the variability and uncertainties in the risk assessment.

To determine the adequacy of the data, the SAB also recommended the development of a system to express the level of confidence associated with various steps in the risk assessment process. The Agency has developed a rating scheme to describe data quality in three areas: interaction, health effects, and exposure. This classification provides a range of five levels of data quality for each of the three areas. Choosing the last level in any area results in declining to perform a quantitative risk assessment due to inadequate data. These last levels are described as follows:

Interactions:

An assumption of additivity cannot be justified, and no quantitative risk assessment can be conducted.

Health effects:

A lack of health effects information on the mixture and its components precludes a quantitative risk assessment.

Exposure:

The available exposure information is insufficient for conducting a risk assessment.

Several commentors, including the SAB, emphasized the importance of not losing these classifications and uncertainties farther along in the risk management process. The discussion of uncertainties has been expanded in the final Guidelines and includes the recommendation that a discussion of uncertainties and assumptions be included at every step of the regulatory process that uses risk assessment.

Another SAB comment was that the Guidelines should include additional procedures for mixtures with more than one end point or effect. The Agency agrees that these are concerns and revised the Guidelines to emphasize these as additional uncertainties worthy of further research.

V. Need for a Technical Support Document

The third major SAB comment concerned the necessity for a separate technical support document for these Guidelines. The SAB pointed out that the scientific and technical background from which these Guidelines must draw their validity is so broad and varied that it cannot reasonably be synthesized within the framework of a brief set of guidelines. The Agency is developing a technical support document that will summarize the available information on health effects from chemical mixtures, and on interaction mechanisms, as well as identify and develop mathematical models and statistical techniques to support these Guidelines. This document will also identify critical gaps and research needs.

Several comments addressed the need for examples on the use of the Guidelines. The Agency has decided to include examples in the technical support document.

Another issue raised by the SAB concerned the identification of research needs. Because little emphasis has been placed on the toxicology of mixtures until recently, the information on mixtures is limited. The SAB pointed out that identifying research needs is critical to the risk assessment process, and the EPA should ensure that these needs are considered in the research planning process. The Agency will include a section in the

technical support document that identifies research needs regarding both methodology and data.

51 FR 34028

GUIDELINES FOR THE HEALTH ASSESSMENT OF SUSPECT DEVELOPMENTAL TOXICANTS

SUMMARY: On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for the Health Assessment of Suspect Developmental Toxicants.

The Guidelines for the Health Assessment of Suspect Developmental Toxicants (hereafter "Guidelines") are intended to guide Agency analysis of developmental toxicity data in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for the Health Assessment of Suspect Developmental Toxicants published November 23, 1984 (49 FR 46324).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

FOR FURTHER INFORMATION CONTACT:

Dr. Carole A. Kimmel
Reproductive Effects Assessment Group
Office of Health and Environmental Assessment (RD-689)
U. S. Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460
202-382-7331

SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process.* In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Work on the Guidelines for the Health Assessment of Suspect Developmental Toxicants began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the field of developmental toxicology from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (49 FR 46324). On November 9, 1984, the Administrator directed that Agency offices use the proposed guidelines in performing risk assessments until final guidelines become available.

After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and preliminary Agency responses to those comments. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for the Health Assessment of Suspect Developmental Toxicants were concurred on in a letter dated July 26, 1985. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The SAB suggested that the Agency pursue additional follow-up work on quantitative risk assessment. Several efforts are currently underway within the Agency on quantitative risk assessment models and procedures, the relationship of maternal and developmental toxicity, and the evaluation and interpretation of postnatal studies. In addition, a document addressing research needs is being prepared to highlight those areas that are in need of further study.

The Agency is continuing to study the risk assessment issues raised in the guidelines and will revise these Guidelines in line with new information as appropriate.

References, supporting documents, and comments received on the proposed
[51 FR 34029]
guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

CONTENTS

Part A: Guidelines for the Health Assessment of Suspect Developmental Toxicants

I. Introduction

These Guidelines describe the procedures that the U.S. Environmental Protection Agency will follow in evaluating potential developmental toxicity associated with human exposure to environmental toxicants. In 1980, the Agency sponsored a conference that addressed issues related to such evaluations (1) and provided some of the scientific basis for these risk assessment Guidelines. The Agency's authority to regulate substances that have the potential to interfere adversely with human development is derived from a number of statutes which are implemented through multiple offices within the Agency. Because many different offices evaluate developmental toxicity, there is a need for intra-Agency consistency in the approach to assess these types of effects. The procedures described here will promote consistency in the Agency's assessment of developmental toxic effects.

The developmental toxicity assessments prepared pursuant to these Guidelines will be utilized within the requirements and constraints of the applicable statutes to arrive at regulatory decisions concerning developmental toxicity. These Guidelines provide a general format for analyzing and organizing the available data for conducting risk assessments. The Agency previously has issued testing guidelines (2, 3) that provide protocols designed to determine the potential of a test substance to induce structural and/or other abnormalities in the developing conceptus. These risk assessment Guidelines do not change any statutory or regulatory prescribed standards for the type of data necessary for regulatory action, but rather provide guidance for the interpretation of studies that follow the testing guidelines, and in addition, provide limited information for interpretation of other studies (e.g., epidemiologic data, functional developmental toxicity studies, and short-term tests) which are not routinely required, but which may be encountered when reviewing data on particular agents. Moreover, risk assessment is just one component of the regulatory process and defines the adverse health consequences of exposure to a toxic agent. The other component, risk management, combines risk assessment with the directives of the enabling regulatory legislation, together with socioeconomic, technical, political, and other considerations, to reach a decision as to whether or how much to control future exposure to the suspected toxic agent. The issue of risk management will not be addressed in these Guidelines.

The background incidence of developmental defects in the human population is quite large. For example, approximately 50% of human conceptuses fail to reach term (4); approximately 3% of newborn children are found to have one or more significant congenital malformations at birth, and by the end of the first postnatal year, about 3% more are found to have serious developmental defects (5, 6). Of these, it is estimated that 20% of human developmental defects are of known genetic transmission, 10% are attributable to known environmental factors, and the remainder result from unknown causes (7). Approximately 7.4% of children are reduced in weight at birth (i.e., below 2500 g) (8). Exposure to agents affecting development can result in multiple manifestations (malformation, functional impairment, altered growth, and/or lethality). Therefore, assessment efforts should encompass a wide array of adverse developmental end points, such as spontaneous abortions, stillbirths, malformations, early postnatal mortality, and other adverse functional or physical changes that are manifested postnatally.

Numerous agents have been shown to be developmental toxicants in animal test systems (9). Several of them have also been shown to be the cause of adverse developmental effects in humans, including alcohol, aminopterin, busulfan, chlorobiphenyls, diethylstilbestrol, isotretinoin, organic mercury, thalidomide, and valproic acid (10, 11, 12, 13). Although a number of agents found to be positive in animal studies have not shown clear evidence of hazard in humans, usually the human data available are inadequate to determine a cause and effect relationship. Comparisons of human and animal data have been made for a limited number of agents that are positive in humans (13, 14). In these comparisons, there was almost always concordance of effects between humans and at least one species tested; also, the minimally effective dose (MED) for the most sensitive animal species was approximately 0.5 to 50 times the human

[51 FR 34030]

MED, not accounting for differences in the incidence of effect at the MED. Thus, there is some limited basis for estimating the risk of exposure to human development based on data from animal studies.

The National Research Council (15) has defined risk assessment as being comprised of some or all of the following components: hazard identification, dose-response assessment, exposure assessment, and risk characterization. In general, the process of assessing the risk of human developmental toxicity may be adapted to this format. However, due to special considerations in assessing developmental toxicity, which will be discussed later in these Guidelines, it is not always possible to follow the exact standards as defined for each component.

Hazard identification is the qualitative risk assessment in which all available experimental animal and human data are used to determine if an agent is likely to cause developmental toxicity. In considering developmental toxicity, these Guidelines will address not only malformations, but

also fetal wastage, growth alteration, and functional abnormalities that may result from developmental exposure to environmental agents.

The dose-response assessment defines the relationship of the dose of an agent and the occurrence of developmental toxic effects. According to the National Research Council (15), this component would usually include the results of an extrapolation from high doses administered to experimental animals or noted in epidemiologic studies to the low exposure levels expected for human contact with the agent in the environment. Since at present there are no mathematical extrapolation models that are generally accepted for developmental toxicity, the Agency, for the most part, uses uncertainty (safety) factors and margins of safety, which will be discussed in these Guidelines. Appropriate models are being sought by the Agency for application to data in this area.

The exposure assessment identifies populations exposed to the agent, describes their composition and size, and presents the types, magnitudes, frequencies, and durations of exposure to the agent.

In risk characterization, the exposure assessment and the dose-response assessment are combined to estimate some measure of the risk of developmental toxicity. As part of risk characterization, a summary of the strengths and weaknesses in each component of the assessment are presented along with major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties.

II. Definitions and Terminology

The Agency recognizes that there are differences in the use of terms in the field of developmental toxicology. For the purposes of these Guidelines the following definitions and terminology will be used.

Developmental Toxicology--The study of adverse effects on the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism. The major manifestations of developmental toxicity include: 1) death of the developing organism, 2) structural abnormality, 3) altered growth, and 4) functional deficiency.

Embryotoxicity and Fetotoxicity--Any toxic effect on the conceptus as a result of prenatal exposure; the distinguishing feature between the two terms is the stage of development during which the injury occurred. The terms, as used here, include malformations and variations, altered growth, and *in utero* death.

Altered Growth--An alteration in offspring organ or body weight or size. Changes in body weight may or may not be accompanied by a change in crown-rump length and/or in skeletal ossification. Altered growth can be induced at any stage of development, may be reversible, or may result in a permanent change.

Functional Developmental Toxicology--The study of the causes, mechanisms, and manifestations of alterations or delays in functional competence of the organism or organ system following exposure to an agent during critical periods of development pre- and/or postnatally.

Malformations and Variations--A malformation is usually defined as a permanent structural change that may adversely affect survival, development, or function. The term teratogenicity, which is used to describe these types of structural abnormalities, will be used in these Guidelines to refer only to structural defects. A variation is used to indicate a divergence beyond the usual range of structural constitution that may not adversely affect survival or health. Distinguishing between variations and malformations is difficult since there exists a continuum of responses from the normal to the extreme deviant. There is no generally accepted classification of malformations and variations. Other terminology that is often used, but no better defined, includes anomalies, deformations, and aberrations.

III. Qualitative Assessment (Hazard Identification of Developmental Toxicants)

Developmental toxicity is expressed as one or more of a number of possible end points that may be used for evaluating the potential of an agent to cause abnormal development. The four types of effects on the conceptus that may be produced by developmental exposure to toxicants include death, structural abnormality, altered growth, and functional deficits. Of these, the first three types of effects are traditionally measured in laboratory animals using the conventional developmental toxicity (also called teratogenicity or Segment II) testing protocol as well as in other study protocols, such as the multigeneration study. Functional deficits are seldom evaluated in routine studies of environmental agents. This section will discuss the end points examined in routinely used protocols as well as the evaluation of data from other types of studies, including functional studies and short-term tests. Transplacental carcinogenesis, another type of developmental effect, will not be discussed in detail here since, at present, it is considered more appropriate to use the Guidelines for Carcinogen Risk Assessment (16) for assessing the human risk for these types of effects. Also, mutational events may occur as part of developmental toxicity, and in practice, are difficult to discriminate from other possible mechanisms of developmental toxicity. The Guidelines for Mutagenicity Risk Assessment (17) should be consulted in cases where genetic damage is suspected.

A. Laboratory Animal Studies of Developmental Toxicity: End Points and Their Interpretation

The most commonly used protocol for assessing developmental toxicity in laboratory animals involves the administration of a test substance to pregnant animals (usually mice, rats, or rabbits) during the period of major organogenesis, evaluation of maternal responses throughout pregnancy, and examination of the dam and the uterine contents just prior to term (2, 3, 18, 19, 20). Other protocols may use exposure periods of one to a few days to investigate periods of particular sensitivity for induction of anomalies in specific organs or organ systems (21).In

[51 FR 34031]

addition, developmental toxicity may be evaluated in studies involving exposure of one or both parents prior to conception, of the conceptus during pregnancy and over several generations, or of offspring during the late prenatal and early postnatal periods. These Guidelines are intended to provide information for interpreting developmental effects related to any of these types of exposure. Since many of the end points evaluated also are related to effects on the parental reproductive systems, these Guidelines will be used in conjunction with those to be published in the future by EPA on male and female reproductive toxicity.

Study designs should include a high dose, which produces some maternal or adult toxicity (i.e., a level which at the least produces marginal but significantly reduced body weight, weight gain, or specific organ toxicity, and at the most produces no more than 10% mortality); a low dose, which demonstrates a no observed effect level (NOEL) for adult and offspring effects; and at least one intermediate dose level. A concurrent control group treated with the vehicle used for agent administration should be included. The route of exposure should be based on expected human exposure considerations, although data from other routes may sometimes be useful, especially if supported by pharmacokinetic information. Test animals should be selected based on considerations of species, strain, age, weight, and health status, and should be randomized to dose groups in order to reduce bias and provide a basis for performing valid statistical tests.

The next three sections discuss individual end points of maternal and developmental toxicity as measured in the conventional developmental toxicity study, the multigeneration study, and, on occasion, in postnatal studies. Other end points specifically related to reproductive toxicity will be covered in the relevant reproductive toxicity guidelines. The fourth section deals with the integrated evaluation of all data, including the relative effects of exposure on maternal animals and their offspring, which is important in assessing the level of concern about a particular agent.

1. End Points of Maternal Toxicity. A number of end points that may be observed as possible indicators of maternal toxicity are listed in Table 1. Maternal mortality is an obvious end point of toxicity; however, a number of other end points can be observed which may give an indication of the subtle effects of an agent. For example, in well-conducted studies, the fertility and gestation indices provide information on the general fertility rate of the animal stock used and are important indicators of toxic effects if treatment begins prior to mating or implantation. Changes in gestation length may indicate effects on the process of parturition.

Table 1.--End Points of Maternal Toxicity

Mortality
Fertility Index (no. with seminal plugs or sperm/no. mated)
Gestation Index (no. with implants/no. with seminal plugs or sperm)
Gestation Length (when allowed to deliver pups)
Body Weight
  Treatment days (at least first, middle, and last treatment days)
  Sacrifice day
Body Weight Change
  Throughout gestation
  During treatment (including increments of time within treatment period)
  Post-treatment to sacrifice
  Corrected maternal (body weight change throughout gestation minus gravid uterine weight or litter weight at sacrifice)
Organ Weights (in cases of suspected specific organ toxicity)
  Absolute
  Relative to body weight
Food and Water Consumption (where relevant)
Clinical Evaluations (on days of treatment and at sacrifice)
  Types and incidence of clinical signs
  Enzyme markers
  Clinical chemistries
Gross Necropsy and Histopathology

Body weight and the change in body weight are viewed collectively as indicators of maternal toxicity for most species, although these end points may not be as useful in rabbits, because body weight changes in rabbits are not good indicators of pregnancy status. Body weight changes may provide more information than a daily body weight measured during treatment or during gestation. Changes in weight during treatment could occur that would not be reflected in the total weight change throughout gestation, because of compensatory weight gain that may occur following treatment but before sacrifice. For this reason, changes in weight during treatment

can be examined as another indicator of maternal toxicity.

Changes in maternal body weight corrected for gravid uterine weight at sacrifice may indicate whether the effect is primarily maternal or fetal. For example, there may be a significant reduction in weight gain throughout gestation and in gravid uterine weight, but no change in corrected maternal weight gain which would indicate primarily an intrauterine effect. Conversely, a change in corrected weight gain and no change in gravid uterine weight suggests primarily maternal toxicity and little or no intrauterine effect. An alternate estimate of maternal weight change during gestation can be obtained by subtracting the sum of the weights of the fetuses. However, this weight does not include the uterine tissue, placental tissue, or the amniotic fluid.

Changes in other end points should also be determined. For example, changes in relative and absolute organ weights may be signs of a maternal effect when an agent is suspected of causing specific organ toxicity. Food and water consumption data are useful, especially if the agent is administered in the diet or drinking water. The amount ingested (total and relative to body weight) and the dose of the agent (relative to body weight) can then be calculated, and changes in food and water consumption related to treatment can be evaluated along with changes in body weight and body weight gain. Data on food and water consumption are also useful when an agent is suspected of affecting appetite, water intake, or excretory function. Clinical evaluations of toxicity may also be used as indicators of maternal toxicity. Daily clinical observations may be useful in describing the profile of maternal toxicity. Enzyme markers and clinical chemistries may be useful indicators of exposure but must be interpreted carefully as to whether or not a change constitutes toxicity. Gross necropsy and histopathology data (when specified in the protocol) may aid in determining toxic dose levels.

2. End Points of Developmental Toxicity. Because the maternal animal, and not the conceptus, is the individual treated during gestation, data generally should be calculated as incidence per litter or as number and percent of litters with particular end points.Table 2 indicates the way in which offspring and litter end points may be expressed.

Table 2.--End Points of Developmental Toxicity.

Litters with implants

- No. implantation sites/dam
- No. corpora lutea (CL)/dam[a]
- Percent preimplantation loss

$$\frac{(\text{CL} - \text{implantations}) \times 100}{\text{CL}}$$[a]

- No. and percent live offspring/litter
- No. and percent resorptions/litter
- No. and percent litters with resorptions

[51 FR 34032]

- No. and percent late fetal deaths/litter
- No. and percent nonlive (late fetal deaths + resorptions) implants/litter
- No. and percent litters with nonlive implants
- No. and percent affected (nonlive + malformed) implants/litter
- No. and percent litters with affected implants
- No. and percent litters with total resorptions
- No. and percent stillbirths/litter

Litters with live offspring[b]

- No. and percent litters with live offspring
- No. and percent live offspring/litter
- Viability of offspring[c]
- Sex ratio/litter
- Mean offspring body weight/litter[c]
- Mean male body weight/litter[c]
- Mean female body weight/litter[c]
- No. and percent externally malformed offspring/litter
- No. and percent viscerally malformed offspring/litter
- No. and percent skeletally malformed offspring/litter
- No. and percent malformed offspring/litter
- No. and percent litters with malformed offspring
- No. and percent malformed males/litter
- No. and percent malformed females/litter
- No. and percent offspring with variations/litter
- No. and percent litters having offspring with variations
- Types and incidence of individual malformations
- Types and incidence of individual variations
- Individual offspring and their malformations and variations (grouped according to litter and dose)
- Clinical signs[c]
- Gross necropsy and histopathology

[a] Important when treatment begins prior to implantation. May be difficult in mice.

[b] Offspring refers both to fetuses observed prior to term or to pups following birth. The end points examined depend on the protocol used for each study.

[c] Measured at selected intervals until termination of the study.

When treatment begins prior to implantation, an increase in preimplantation loss could indicate an adverse effect either on the developing blastocyst or on the process of implantation itself. If treatment begins around the time of implantation (i.e., day 6 of gestation in the mouse, rat, or rabbit), an increase in preimplantation loss probably reflects normal variability in the animals being used, but the data should be examined carefully to determine whether or not the effect is dose related. If preimplantation

loss is related to dose in either case, further studies would be necessary to determine the mechanism and extent of such effects.

The number and percent of live offspring per litter, based on all litters, may include litters that have no live implants. The number and percent resorptions or late fetal deaths per litter gives some indication of when the conceptus died, and the number and percent nonlive implants per litter (postimplantation loss) is a combination of resorptions and late fetal deaths. The number and percent of litters showing an increased incidence for these end points is generally useful but may be less useful than incidence per litter because, in the former case, a litter is counted whether it has one or all resorbed, dead, or nonlive implants.

If a significant increase in postimplantation loss is found after exposure to an agent, the data may be compared not only with concurrent controls, but also with recent historical control data, since there is considerable interlitter variability in the incidence of postimplantation loss (22). If a given study control group exhibits an unusually high or low incidence of postimplantation loss compared to historical controls, then scientific judgment must be used to determine the adequacy of the studies for risk assessment purposes.

The end point for affected implants (i.e., the combination of nonlive and malformed conceptuses) gives an indication of the total intrauterine response to an agent and sometimes reflects a better dose-response relationship than does the incidence of nonlive or malformed offspring taken individually. This is especially true at the high end of the dose-response curve in cases when the incidence of nonlive implants per litter is greatly increased. In such cases, the malformation rate may appear to decrease because only unaffected offspring have survived. If the incidence of prenatal death or malformation is unchanged, then the incidence of affected implants will not provide any additional dose-response information. In studies where maternal animals are allowed to deliver pups normally, the number of stillbirths per litter should also be noted.

The number of live offspring per litter, based on those litters that have one or more live offspring, may be unchanged even though the incidence of nonlive in all litters is increased. This could occur either because of an increase in the number of litters with no live offspring, or an increase in the number of implants per litter. A decrease in the number of live offspring per litter should be accompanied by an increase in the incidence of nonlive implants per litter, unless the implant numbers differ among dose groups. In postnatal studies, the viability of live born offspring should be determined at selected intervals until termination of the study.

The sex ratio per litter, as well as the body weights of males and females, can be examined to determine whether or not one sex is preferentially affected by the agent. However, this is an unusual occurrence.

A change in offspring body weight is a sensitive indicator of developmental toxicity, in part because it is a continuous variable. In some cases, offspring weight reduction may be the only indicator of developmental toxicity; if so, there is always a question remaining as to whether weight reduction is a permanent or transitory effect. A permanent weight change may be considered more severe than a transitory change, although little is known about the long-term consequences of short-term fetal or neonatal weight changes. When fetal or neonatal weight reduction is the only indicator of developmental toxicity, data from the two-generation reproduction study (2), if available, may be useful for evaluating these parameters. Ideally, follow-up studies to evaluate postnatal viability, growth, and survival through weaning should be conducted. There are other factors that should be considered in the evaluation of fetal or neonatal weight changes. For example, in polytocous animals, fetal and neonatal weights are usually inversely correlated with litter size, and the upper end of the dose-response curve may be confounded by smaller litters and increased fetal or neonatal weight. Additionally, the average body weight of males is greater than that of females in the more commonly used laboratory animals.

Live offspring should be examined for external, visceral, and skeletal malformations. If only a portion of the litter is examined, then it is preferable that those examined be randomly selected from each litter. An increase in the incidence of malformed offspring may be indicated by a change in one or more of the following end points: the incidence of malformed offspring per litter, the number and percent of litters with malformed offspring, or the number of offspring or litters with a particular malformation that appears to increase with dose as indicated by the incidence of individual types of malformations.

[51 FR 34033]

Other ways of examining the data include the incidence of external, visceral, and skeletal malformations which may indicate which general systems are affected. A listing of individual offspring with their malformations and variations may give an indication of the pattern of developmental deviations. All of these methods of expressing and examining the data are valid for determining the effects of an agent on structural development. However, care must be taken to avoid counting offspring more than once in evaluating any single end point based on number or percent of offspring or litters. The incidence of individual types of malformations and variations should be examined

for significant changes which may be masked if the data on all malformations and variations are pooled. Appropriate historical control data are helpful in the interpretation of malformations and variations, especially those that normally occur at a low incidence apparently unrelated to dose in an individual study. Although a dose-related increase in malformations is interpreted as an adverse developmental effect of exposure to an agent, the significance of anatomical variations is more difficult to determine, and must take into account what is known about developmental stage (e.g., with skeletal ossification), background incidence of certain variations (e.g., 12 or 13 pairs of ribs in rabbits), or other strain - or species-specific factors. However, if variations are significantly increased in a dose-related manner, these should also be evaluated as a possible indication of developmental toxicity. The Interagency Regulatory Liaison Group noted that dose-related increases in defects, which may occur spontaneously, are as relevant as dose-related increases in any other developmental toxicity end points (23).

3. *Functional Developmental Toxicology.* Developmental effects, which are inducible by exogenous agents, are not limited to death, structural abnormalities, and altered growth. Rather, it has been demonstrated in a number of instances that subtle alterations in the functional competence of an organ or a variety of organ systems may result from exposure during critical developmental periods that may occur between conception and sexual maturation. Often, these functional defects are observed at dose levels below those at which gross malformations are evident (24). At present, such testing is not routinely required in the United States. However, data from postnatal studies, when available, are considered very useful for the assessment of the relative importance and severity of findings in the fetus and neonate. Often, the long-term consequences of adverse developmental outcomes at birth are unknown, and further data on postnatal development and function may contribute valuable information. When regulatory statutes permit, studies designed to evaluate adverse fetal or neonatal outcomes have been requested (e.g., the Office of Pesticide Programs has sometimes requested postnatal studies where the reversibility of study findings were at issue). In some cases, useful data can be derived from well-executed multigeneration studies.

Much of the early work in functional developmental toxicology was related to behavioral evaluations, and the term "behavioral teratology" became prominent in the mid 1970s. Less work has been done on other functional systems, but sufficient data have accumulated to indicate that the cardiopulmonary, immune, endocrine, digestive, urinary, nervous, and reproductive systems are subject to alterations in functional competence (25, 26). Currently, there are no standard testing procedures, although some attempts are being made to standardize and evaluate tests and protocols (27). The functional evaluation of specific systems often involves highly specialized training and equipment. The routine use of such test procedures may not always be practical, but may be extremely important in determining the nature of a suspected alteration in terms of its biological significance and dose-response relationship.

The interpretation of data from functional developmental toxicology studies is limited due to the lack of knowledge about the underlying toxicological mechanisms and their significance. However, since such data are sometimes encountered in the risk assessment of particular agents, some guidance is provided here concerning general concepts of study design and evaluation.

a. Several aspects of study design are similar to those important in standard developmental toxicity studies (e.g., a dose-response approach with the highest dose producing minimal overt maternal or perinatal toxicity, number of litters large enough for adequate statistical power, randomization of animals to dose groups, litter generally considered the statistical unit, etc.).

b. A replicate study design provides added confidence in the interpretation of data.

c. Use of a pharmacological challenge may be valuable in evaluating function and "unmasking" effects not otherwise detectable, particularly in the case of organ systems that are endowed with a reasonable degree of functional reserve capacity.

d. Use of functional tests with a moderate degree of background variability may be more sensitive to the effects of an agent than are tests with low variability that may be impossible to disrupt without being life-threatening. Butcher et al. (28) have discussed this with relation to behavioral end points.

e. A battery of functional tests usually provides a more thorough evaluation of the functional competence of an animal; tests conducted at several ages may provide more information about maturational changes.

f. Critical periods for the disruption of functional competence include both the prenatal and the postnatal periods to the time of sexual maturation, and the effect is likely to vary depending on the time and degree of exposure.

Although interpretation of functional data may be difficult at present, there are at least three ways in which the data from these studies may be useful for risk assessment purposes: 1) to help elucidate the long-term consequences of fetal and neonatal findings; 2) to indicate the potential for an agent to cause functional alterations, and the effective doses relative to those that produce other forms of toxicity;

and 3) for existing environmental agents, to focus on organ systems to be evaluated in exposed human populations.

4. *Overall Evaluation of Maternal and Developmental Toxicity.* As discussed previously, individual end points are evaluated in developmental toxicity studies, but an integrated evaluation must be done considering all maternal and developmental end points in order to interpret the data fully. Developmental toxicity is considered to be an increase in the incidence of malformed offspring, decreased viability (prenatal or postnatal), altered growth, and/or functional deficits.

The level of concern for a developmental toxic effect is related to several issues, including the relative toxicity of an agent to the offspring versus the adult animal, and the long-term consequences of findings in the fetus or neonate. Those agents which produce developmental toxicity at a dose that is not toxic to the maternal animal are of greatest concern because the developing organism appears to be selectively affected or more sensitive than the adult. However, when developmental effects are produced only

[51 FR 34034]

at maternally toxic doses, the types of developmental effects should be examined carefully, and not discounted as being secondary to maternal toxicity. Current information is inadequate to assume that developmental effects at maternally toxic doses result only from the maternal toxicity; rather, when the lowest observed effect level is the same for the adult and developing organisms, it may simply indicate that both are sensitive to that dose level. Moreover, the maternal effects may be reversible while effects on the offspring may be permanent. These are important considerations for agents to which humans may be exposed at minimally toxic levels either voluntarily or in the workplace, since several agents are known to produce adverse developmental effects at minimally toxic doses in adult humans (e.g., smoking, alcohol).

Approaches for ranking agents for their selective developmental toxicity are being developed; Schardein (10) has reviewed several of these. Of current interest are approaches that develop ratios relating an adult toxic dose to a developmental toxic dose (29, 30, 31, 32). Ratios near unity indicate that developmental toxicity occurs only at doses producing maternal toxicity; as the ratio increases, there is a greater likelihood of developmental effects occurring without maternal manifestations. Although further exploration and validation are necessary, such approaches may ultimately help in identifying those agents that pose the greatest threat and should be given higher priority for further testing (33).

5. *Short-term Testing in Developmental Toxicity.* The need for short-term tests for developmental toxicity has arisen from the large number of agents in or entering the environment, the interest in reducing the number of animals used for routine testing, and the expense of testing. Two approaches are considered here in terms of their contribution to the overall testing process: 1) an *in vivo* mammalian screen, and 2) a variety of *in vitro* systems. Currently, neither approach is considered as a replacement for routine *in vivo* developmental toxicity testing in experimental animals, and should not be used to make the final decision as to whether an agent is a positive or negative developmental toxicant; rather, such tests may be useful as tools for assigning priorities for further, more extensive testing. Although such short-term tests are not routinely required, data are sometimes encountered in the review of chemicals; the comments are provided here for guidance in the evaluation of such data.

a. *In Vivo* Mammalian Developmental Toxicity Screen. The most widely studied *in vivo* approach is that developed by Chernoff and Kavlock (34) which uses the pregnant mouse. This approach is based on the hypothesis that a prenatal injury, which results in altered development, will be manifested postnatally as reduced viability and/or impaired growth. In general, the test substance is administered over the period of major organogenesis at a single dose level that will elicit some degree of maternal toxicity. A second lower dose level may be used which potentially will reduce the chances of false positive results. The pups are counted and weighed shortly after birth, and again after 3-4 days. End points that are considered in the evaluation include: general maternal toxicity (including survival and weight gain), litter size, and viability, weight, and gross malformations in the offspring. Basic priority-setting categories for more extensive testing have been suggested: 1) agents that induce perinatal death should receive highest priority, 2) agents inducing perinatal weight changes should be ranked lower in priority, and 3) agents inducing no effect should receive the lowest priority (34). Another scheme that has been proposed applies a numerical ranking to the results as a means of prioritizing agents for further testing (35, 36).

The mouse was chosen originally for this test because of its low cost, but the procedure should be easily applicable to other species. However, the test will only predict the potential for developmental toxicity of an agent in the species utilized and does not improve the ability to extrapolate risk to other species, including humans. The Office of Toxic Substances has developed testing guidelines for this procedure (37). Although the testing guidelines are available, such procedures are not routinely

required, and further validation is currently being carried out (38).

b. *In Vitro* Developmental Toxicity Screens. Test systems that fall under the general heading of "*in vitro*" developmental toxicity screens include any system that employs a test subject other than the intact pregnant mammal. These systems have long been used to assess events associated with normal and abnormal development, but only recently have they been considered for their potential as screens in testing (39, 40, 41). Many of these systems are now being evaluated for their ability to predict the developmental toxicity of various agents in intact mammalian systems. This validation process requires certain considerations in study design, including defined end points for toxicity and an understanding of the system's ability to handle various test agents (40, 42). A list of agents for use in such validation studies has been developed (43).

6. *Statistical Considerations.* In the assessment of developmental toxicity data, statistical considerations require special attention. Since the litter is generally considered the experimental unit in most developmental toxicity studies, the statistical analyses should be designed to analyze the relevant data based on incidence per litter or on the number of litters with a particular end point. The analytical procedures used and the results, as well as an indication of the variance in each end point, should be clearly indicated in the presentation of data. Analysis of variance (ANOVA) techniques, with litter nested within dose in the model, take the litter variable into account but allow use of individual offspring data and an evaluation of both within and between litter variance as well as dose effects. Nonparametric and categorical procedures have also been widely used for binomial or incidence data. In addition, tests for dose-response trends can be applied. Although a single statistical approach has not been agreed upon, a number of factors important in the analysis of developmental toxicity data have been discussed (23, 44).

Studies that employ a replicate experimental design (e.g., two or three replicates with 10 litters per dose per replicate rather than a single experiment with 20-30 litters per dose group) allow for broader interpretation of study results since the variability between replicates can be accounted for using ANOVA techniques. Replication of effects due to a given agent within a study, as well as between studies or laboratories, provides added strength in the use of data for the estimation of risk.

An important factor to determine in evaluating data is the power of a study (i.e., the probability that a study will demonstrate a true effect), which is limited by the sample size used in the study, the background incidence of the end point observed, the variability in the incidence of the end point, and the analysis method. As an example, Nelson and Holson (45) have shown that the number of litters needed to detect a 5 or 10% change was dramatically lower for fetal weight (a continuous variable with low variability) than for resorptions (a binomial response with high variability). With the current recommendation in

[51 FR 34035]

testing protocols being 20 rodents per dose group (2, 3), it is possible to detect an increased incidence of malformations in the range of 5 to 12 times above control levels, an increase of 3 to 6 times the *in utero* death rate, and a decrease of 0.15 to 0.25 times the fetal weight. Thus, even within the same study, the ability to detect a change in fetal weight is much greater than for the other end points measured. Consequently, for statistical reasons only, changes in fetal weight are often observable at doses below those producing other signs of developmental toxicity. Any risk assessment should present the detection sensitivity for the study design used and for the end point(s) evaluated.

Although statistical analyses are important in determining the effects of a particular agent, the biological significance of data should not be overlooked. For example, with the number of end points that can be observed in developmental toxicity studies, a few statistically significant differences may occur by chance. On the other hand, apparent trends with dose may be biologically relevant even though statistical analyses do not indicate a significant effect. This may be true especially for the incidence of malformations or *in utero* death where a relatively large difference is required to be statistically significant. It should be apparent from this discussion that a great deal of scientific judgment based on experience with developmental toxicity data and with principles of experimental design and statistical analysis may be required to adequately evaluate such data.

B. Human Studies

Because of the ethical considerations involved, studies with deliberate dosing of humans are not done. Therefore, dose-effect developmental toxicity data from humans are limited to those available from occupational, environmental, or therapeutic exposures. While animal studies provide dose-response data that can be used in the extrapolation of risk to humans, good epidemiologic data provide the best information for assessing human risk.

The category of "human studies" includes both epidemiologic studies and other reports of cases or clusters of events. While case reports have been important in identifying several human teratogens, they are potentially of greater value in identifying topics for further investigation (46). The data from case reports are often of an anecdotal or highly selected nature, and thus are of limited usefulness for risk assessment except when a unique defect is produced, as with thalidomide, or when the agent is

so potent as to greatly increase the incidence of a particular defect(s).

As there are many different designs for epidemiologic studies, simple rules for their evaluation do not exist. The assessment of epidemiologic studies requires a sophisticated level of understanding of the appropriate epidemiologic and statistical methods and interpretation of the findings. Factors that increase a study's usefulness for risk assessment include such things as the examination of multiple end points and exposure levels, the validity of the data, and proper control of other risk factors, effect modifiers, and confounders in the study design and/or analysis. A more in-depth discussion can be found elsewhere (47).

As described earlier, a single developmental toxicant can result in multiple end points (malformations, functional impairment, altered growth, and/or lethality). These end points can be thought of as sequential competing risks. For example, a malformed fetus spontaneously aborted would not be observed in a study of births with malformations (48). Very early conceptus losses may not be identified in human populations, whereas in most laboratory animal studies, all resorption sites can be identified. Many epidemiologic studies, especially of the case-control design, have focused on one end point, possibly missing a true effect of exposure. Furthermore, some studies have selected one type or class of malformations to study. Since an agent can result in different spectra of malformations following exposure at different times in the pregnancy (49), limiting a study to one class of malformation may give misleading results. Malformations can be meaningfully grouped only if there is a logical underlying teratogenic mechanism or pathogenetic pathway. As a minimum, malformations, deformations, and disruptions should be separated.

The power, or probability of a study to detect a true effect, is dependent upon the size of the study group, the frequency of the outcome in the general population, and the level of excess risk to be identified. Rarer outcomes, such as malformations, require thousands of pregnancies to have a high probability of detecting an increase in risk. More common outcomes, such as fetal loss, require hundreds of pregnancies to have the same probability (8, 23, 50, 51, 52, 53). The confidence one has in the results of a study with negative findings is directly related to the power of the study to detect clinically meaningful differences in incidence for the end points studied.

As in animal studies, pregnancies within the same family (or litter) are not independent events. In animal studies, the litter is generally used as the unit of measure. This approach is difficult in humans since the pregnancies are sequential, with the risk factors changing for the different pregnancies (23, 51, 54). If more than one pregnancy per family is included, and this is often necessary due to small study groups, the use of non-independent observations overestimates the true size of the population at risk and artificially increases the significance level (54).

Other criteria for evaluating epidemiologic studies include the following (23, 50, 52, 55, 56, 57, 58):

1. The potential for complete or relatively complete ascertainment of events for study. This can vary by outcome and by data source; for example, if hospital records are used, early fetal losses will be underascertained, but a more complete list of pregnancies could be obtained by interviewing the women. Congenital malformations can be more completely ascertained using hospital records than birth certificates. Studies with relatively complete ascertainment of events, or at least low probability of unbiased ascertainment, should carry more weight.

2. Validity (accuracy) of the data. Recall of past events in interviews may be faulty, while hospital files contain data recorded at the time of the event (but may be incomplete). Validation of interview data with an independent source, where possible, increases confidence in the results of the study.

3. Collection of data on other risk factors, effect modifiers, and confounders. Data on smoking, alcohol consumption, drug use, and environmental and occupational exposure, etc., during pregnancy should be examined and controlled for in the study design and/or analysis where appropriate. The analytic techniques used to control for these factors require careful consideration in their application and interpretation.

C. Other Considerations

1. *Pharmacokinetics.* Extrapolation of data between species can be aided considerably by the availability of data on the pharmacokinetics of a particular agent in the species tested and, if possible, in humans. Information on half-lives, placental metabolism and transfer, and concentrations of the parent compound and metabolites in the

[51 FR 34036]

maternal animal and conceptus may be useful in predicting risk for developmental toxicity. Such data may also be helpful in defining the dose-response curve, developing a more accurate comparison of species sensitivity including that of humans (59, 60), determining dosimetry at target sites, and comparing pharmacokinetic profiles for various dosing regimens or routes of exposure. Pharmacokinetic studies in developmental toxicology are most useful if conducted in pregnant animals at the stage when developmental insults occur. The correlation of pharmacokinetic parameters and developmental toxicity data may be

useful in determining the contribution of specific pharmacokinetic parameters to the effects observed (61).

2. *Comparisons of Molecular Structure.* Comparisons of the chemical or physical properties of an agent with those of known developmental toxicants may provide some indication of a potential for developmental toxicity. Such information may be helpful in setting priorities for testing of agents or for evaluation of potential toxicity when only minimal data are available. Structure/activity relationships have not been well studied in developmental toxicology, although data are available that suggest structure-activity relationships for certain classes of chemicals (e.g., glycol ethers, steroids, retinoids). Under certain circumstances (e.g., in the case of new chemicals), this is one of several procedures used to evaluate the potential for toxicity when little or no data are available.

D. Weight-of-Evidence Determination

Information available from studies discussed previously, whether indicative of potential concern or not, must be evaluated and factored into the risk assessment. The types of data may vary from chemical to chemical, and certain types of data may be more relevant than other types in performing developmental toxicity assessments. The primary considerations are the human data (which are seldom available) and the experimental animal data. The qualitative assessment for developmental toxicity should include statements concerning the quality of the data, the resolving power of the studies, the number and types of end points examined, the relevance of route and timing of exposure, the appropriateness of the dose selection, the replication of the effects, the number of species examined, and the availability of human case reports, case series, and/or epidemiologic study data. In addition, pharmacokinetic data and structure-activity considerations, as well as other factors that may affect the quality, should be taken into account. Therefore, all data pertinent to developmental toxicity should be examined in the evaluation of a chemical's potential to cause developmental toxicity in humans, and sound scientific judgment should be exercised in interpreting the data in terms of the risk for adverse human developmental health effects.

IV. Quantitative Assessment

Risk assessment involves the description of the nature and often the magnitude of potential human risk, including a description of any attendant uncertainty. In the final phase of the risk assessment (risk characterization), the results of the qualitative evaluation (hazard identification), the dose-response, and the exposure assessments are combined to give qualitative and/or quantitative estimates of the developmental toxicity risk. A summary of the strengths and weaknesses of the hazard identification, dose-response assessment, and exposure assessment should be discussed. Major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties in the assessment also should be presented.

A. Dose-Response Assessment

When quantitative human dose-effect data are available and with sufficient range of exposure, dose-response relationships may be examined. However, such data have rarely been available; thus, other methods have been used in developmental toxicology for estimating exposure levels that are unlikely to produce adverse effects in humans. The dose-response assessment is usually based on the evaluation of tests performed in laboratory animals. Evidence for a dose-response relationship is an important criterion in the assessment of developmental toxicity, although this may be based on limited data from standard three-dose studies. As mentioned earlier (section III. A. 2.), however, traditional dose-response relationships may not always be observed for some end points. For example, as the exposure level rises, embryo/fetolethal levels may be reached, resulting in an observed decrease in malformations with increasing dose (49, 51). The potential for this relationship indicates that dose-response relationships for individual end points as well as combinations of end points (e.g., dead and malformed combined) must be carefully examined and interpreted.

Although dose-response data are important in this area, the approaches frequently employed in attempts to extrapolate to humans has involved simply the use of uncertainty (safety) factors and margins of safety, which in some respects are conceptually similar. However, uncertainty factors and margins of safety are computed differently and are often used in different regulatory situations. The choice of approach is dependent upon many factors, including the statute involved, the situation being addressed, the data base used, and the needs of the decision-maker. The final uncertainty factor used and the acceptability of the margin of safety are risk management decisions, but the scientific issues that must be taken into account are addressed here.

The uncertainty factor approach results in a calculated exposure level believed to be unlikely to cause any toxic developmental response in humans. The size of the uncertainty factor will vary from agent to agent and will require the exercise of scientific judgment (10, 62), taking into account interspecies differences, the nature and extent of human exposure, the slope of the dose-response curve, the types of developmental effects observed, and the relative dose levels for maternal and developmental toxicity in the test species. The uncertainty factor selected is then divided into the NOEL for the most sensitive end point obtained from

the most appropriate and/or sensitive mammalian species examined to obtain an acceptable exposure level. Currently, there is no one laboratory animal species that can be considered most appropriate for predicting risk to humans (10). Each agent should be considered on a case-by-case basis.

The margin of safety approach derives a ratio of the NOEL from the most sensitive species to the estimated human exposure level from all potential sources (63). The adequacy of the margin of safety is then considered, based on the weight of evidence, including the nature and quality of the hazard and exposure data, the number of species affected, dose-response relationships, and other factors such as benefits of the agent.

Although the standard study design for a developmental toxicity study calls for a low dose that demonstrates a NOEL, there may be circumstances where a risk assessment is based on the results of a study in which a NOEL for developmental toxicity could not be identified. Rather, the lowest dose administered caused significant effect(s) and was identified as the lowest observed effect level (LOEL). In circumstances where only a LOEL is available, it may be appropriate to apply

[51 FR 34037]

an additional uncertainty factor. The magnitude of this additional factor is dependent upon scientific judgment. In some instances, additional studies may be needed to strengthen the confidence in this additional uncertainty factor.

B. Exposure Assessment

The results of the dose-response assessment are combined with an estimate of human exposure in order to obtain a quantitative estimate of risk. The Guidelines for Estimating Exposures are published separately (64) and will not be discussed in detail here. In general, the exposure assessment describes the magnitude, duration, schedule, and route of exposure. This information is developed from monitoring data and from estimates based on modeling of environmental exposures. Unique considerations relevant to developmental toxicity are duration and period of exposure as related to stage of development (i.e., critical periods), and the possibility that a single exposure may be sufficient to produce adverse developmental effects (i.e., chronic exposure is not a necessary prerequisite for developmental toxicity to be manifested). Also, it should be recognized that exposure of almost any segment of the human population (i.e., fertile men and women, the conceptus, and the child up to the age of sexual maturation) may lead to risk to the developing organism.

Data on exposure to humans may be qualitative or quantitative. The qualitative data could be surrogate data, such as employment or residence histories; quantitative or dose data are frequently not available. Exposures at different stages of the reproductive process can result in different outcomes (49). In laboratory studies, these time periods can be carefully controlled. In human studies, especially retrospective ones, linking of specific time periods and specific exposures, even on a qualitative level, may be difficult due to errors of recall or record keeping (where records are available). The increased probability of misclassification of exposure status may affect the ability of a study to recognize a true effect (8, 23, 52, 65, 66).

Exposure may be defined at a specific point in time, or the cumulative lifetime exposure up to a specific point in time. Each of these definitions carries an implicit assumption about the underlying relationship between exposure and outcome. For example, a cumulative exposure measure assumes that total lifetime exposure is important, with a greater probability of effect with greater total exposure; a dichotomous exposure measure (ever exposed versus never exposed) assumes an irreversible effect of exposure; and exposure at a specific time in the reproductive process assumes that only concurrent exposure is important. The appropriate exposure depends on the outcome(s) studied, the biologic mechanism affected by exposure, and the half-life of the exposure. Unbiased misclassification of exposure, due either to poor data or to an inappropriate exposure variable, may result in missing an effect of the agent under study.

C. Risk Characterization

Many uncertainties have been pointed out in these Guidelines which are associated with the toxicological and exposure components of risk assessments in developmental toxicology. In the past, these uncertainties have often not been readily apparent or consistently presented. The presentation of any risk assessment for developmental toxicity should be accompanied by statements concerning the strength of the hazard evaluation (see section III. D. for more detail) as well as dose-response relationships, estimates of human exposure, and any other factors that affect the quality and precision of the assessment. The dose-response and exposure data are combined to estimate risk based on a NOEL for any adverse developmental effect. The uncertainty factor selected or margin of safety calculated should be sufficiently qualified as to the assumptions used and the accuracy of the estimates.

At present, there are no mathematical models that are generally accepted for estimating developmental toxicity responses below the applied dose range. This is due primarily to a lack of understanding of the biological mechanisms underlying developmental toxicity, intra/interspecies differences in the types of developmental events, the influence of maternal effects on the dose-response curve, and whether or not a threshold exists below which no effect will be

produced by an agent. Many developmental toxicologists assume a threshold for most developmental effects; this assumption is based largely on the biological rationale that the embryo is known to have some capacity for repair of the damage or insult (49), and that most developmental deviations are probably multifactorial in nature (67). The existence of a NOEL in an animal study does not prove or disprove the existence or level of a true threshold; it only defines the highest level of exposure under the conditions of the test that are not associated with a significant increase in effect. The use of NOELs and uncertainty factors or margins of safety are attempts to ensure that the allowable levels are below those that will produce a significant increase in developmental effects.

Discussions of risk extrapolation procedures have noted that further work is needed to improve mathematical tools for developing estimates of potential human developmental risk (62, 68). Gaylor (69) has suggested an approach for controlling risk that combines the use of mathematical models for low-dose estimation of risk with the application of an uncertainty factor based on a preselected level of allowable risk. This approach is similar to approaches proposed for carcinogenesis, but does not preclude the possibility of a threshold, and may provide a more quantitative approach to controlling risk. Several such approaches are being examined. For the most part, the Agency will continue to use uncertainty factors and margins of safety as described above. Other appropriate methods for expressing risk are being sought and will be applied if considered acceptable.

These Guidelines summarize the procedures that the U.S. Environmental Protection Agency will follow in evaluating the potential for agents to cause developmental toxicity. These Guidelines will be reviewed and updated as advances are made in the field, since it is evident that our ability to evaluate and predict human developmental toxicity is imprecise. Further studies that 1) delineate the mechanisms of developmental toxicity and pathogenesis, 2) provide comparative pharmacokinetic data, and 3) elucidate the functional modalities that may be altered by exposure to toxic agents will aid in the interpretation of data and interspecies extrapolation. These types of studies, along with further evaluation of the relationship between maternal and fetal toxicity and the concept of a threshold in developmental toxicity, will provide for the development of improved mathematical models to more precisely assess risk.

V. References

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[51 FR 34038]

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[51 FR 34039]

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Part B: Response to Public and Science Advisory Board Comments

I. Introduction

This section summarizes some of the issues raised in public comments on the Proposed Guidelines for the Health Assessment of Suspect Developmental Toxicants published November 23, 1984 (49 FR 46324). Comments were received from 44 individuals or organizations. The Agency's initial summary of comments was presented to the Developmental Toxicity Guidelines Panel of the Science Advisory Board (SAB) at its organizational meeting on March 4, 1985. At its April 22-23, 1985, meeting, the Panel provided the Agency with its suggestions and recommendations concerning the Guidelines.

The SAB and public comments were diverse and addressed issues from a variety of perspectives. In general, the comments were favorable and in support of the Guidelines. The SAB Panel noted that the field of developmental toxicology is particularly weak with respect to quantitative assessment and recommended that further efforts be given to developing alternative methods for quantitative estimates of risk for developmental toxicity. They also indicated that further discussion of the relationship of maternal toxicity to fetal toxicity could be added. Concern was expressed that these Guidelines be coordinated with the reproductive toxicity guidelines which are currently being developed.

In response to the comments, the Agency has modified or clarified many sections of the Guidelines. For purposes of this discussion, only the most significant issues reflected by the public and SAB comments are discussed. Several minor recommendations, which do not warrant discussion here, were considered by the Agency in the revision of these Guidelines.

II. Coordination With Other Guidelines

A. Other Risk Assessment Guidelines

Several commentors raised concerns about aspects of developmental toxicity (e.g., paternally-mediated effects, effects of subchronic exposures, transplacental carcinogenesis, etc.) that were not covered in these Guidelines, and how these Guidelines will integrate with those on male and female reproductive toxicity which are still under development.

The Guidelines have been revised to indicate that developmental toxicity may result from several different types of exposure, including parental exposure prior to conception, acute or subacute exposure during organogenesis, perinatal and postnatal development to the time of sexual maturation, or subchronic exposure as would be the case in multigeneration studies. These Guidelines provide information for interpreting developmental effects related to any of the types of exposure mentioned above. End points of developmental toxicity, which are measured in multigeneration studies, have been added to Table 2 and discussed in the text. Transplacental carcinogenesis, although considered a developmental effect, will be evaluated and assessed in terms of human risk according to the Guidelines for Carcinogen Risk Assessment. Careful attention will be paid to integrating these developmental toxicity risk assessment Guidelines and the male and female reproductive toxicity risk assessment guidelines, which are currently being written, so that overlapping material is not in conflict, and no pertinent information is overlooked. Since the developmental and reproductive toxicity guidelines are being developed by Agency committees that have overlapping membership within the Agency, such integration will be ensured.

B. Coordination With Testing Guidelines

Several commentors indicated that these Guidelines did not make clear enough the fact that testing guidelines are already in place and that these guidelines were intended only for the purposes of risk assessment.

The Guidelines have been revised to indicate that they do not constitute any changes in current testing guidelines, but rather they are intended to provide guidance for the interpretation of studies that follow the testing guidelines. In addition, limited information is provided for interpretation of other studies (e.g., functional developmental toxicity studies and short-term tests) which are not routinely required or for which there are no current testing guidelines, but which may be encountered when reviewing data on particular agents.

III. Definitions

Several questions were raised about definitions of terminology, due to lack of clarity or inconsistency with other parts of these Guidelines or the testing guidelines.

As indicated in the Guidelines, there are differences in the use of terms in the field of developmental toxicology, and the terms have been defined so that the reader may understand how the terms are being used. Several minor changes in the definitions have been made

[51 FR 34040]

to make them more consistent. For example, the definition for developmental toxicology has been expanded to include the wide range of exposure situations that may result in developmental effects. The term functional teratology has been changed to functional developmental toxicology, and the term

teratogenicity has been discussed in the section on malformations and variations.

IV. Qualitative Assessment

A. Maternal and Developmental Toxicity

Several commentors noted the need for a better discussion of how maternal toxicity affects the evaluation of developmental toxic effects.

The Agency has taken the approach in these Guidelines of discussing in detail the individual end points of maternal and offspring toxicity, then giving guidance relating to an overall evaluation of the data in Part A, section III.A.4. This approach is consistent with the philosophy reflected in the Guidelines as follows: Those agents that cause developmental effects at doses lower than those causing maternal toxicity are of greatest concern, but developmental effects at doses that also produce maternal toxicity shoud not be discounted as secondary to maternal effects. Rather, when the lowest observed effect level (LOEL) is the same for maternal and developmental toxicity, it may indicate similar sensitivities to the agent, and maternal effects may be reversible while developmental effects may be permanent.

B. Functional Developmental Toxicity

Several commentors raised concern about the premature use of functional data in the risk assessment process. On the other hand, the SAB Panel felt that these tests were very valuable in assessing developmental toxicity.

The Agency does not routinely require such testing, and these Guidelines do not suggest requirements. However, in the review of data on existing chemicals, such data are sometimes encountered and must be evaluated by the Agency. The discussion in the Guidelines is intended to delineate the current state of the art, and to indicate to what extent the data currently may be used for risk assessment purposes.

C. Short-Term Testing

Several commentors stressed the need for further refinement, validation, and comparative testing to determine the credibility of short-term tests for developmental toxicity. The appropriateness of single dose level screens for the purpose of prioritization was endorsed by the SAB Panel with the reservation that too many false positives might occur, and that positive agents in these screens would be permanently labelled as positive developmental toxicants.

Since data from these types of test procedures may be encountered in the assessment of chemicals, the Agency felt it appropriate to give guidance as to how these should be evaluated. The Guidelines have been revised to clearly indicate that these tests are not routinely required, shoud not be considered as a replacement for routine *in vivo* developmental toxicity testing in mammals, and should not be used to make the final decision as to whether an agent is a positive or negative developmental toxicant.

D. Comparisons of Molecular Structure

Comments suggested that not much is known about structure-activity relationships for developmental toxicants, and that this procedure should not be used except in the case of hormone analogs.

A statement has been added to indicate that structure-activity relationships have not been well-studied in developmental toxicology, but under certain circumstances, e.g., in the case of the premanufacturing notice process (TSCA, section 5), the evaluation of molecular structure is one of several procedures used by the Agency to evaluate potential toxicity and to support requests for testing of new chemicals.

V. Quantitative Assessment

Most comments related to the appropriateness of using uncertainty (safety) factors, margins of safety, and no observed effect levels (NOELs). Some commentors felt that the concept of threshold was not adequately discussed in the Guidelines.

These Guidelines are intended to reflect current Agency policy and practice. Although more quantitative assessment of developmental toxicity data are desirable, and efforts are currently ongoing within the Agency to evaluate other approaches, the current practice is to use the NOEL (or the LOEL if a NOEL is not available), and to apply an uncertainty factor or to calculate the margin of safety. This practice is based in large part on the lack of understanding of the biological mechanisms involved. The uncertainty factor used or acceptability of the margin of safety are considered risk management decisions, but the scientific issues that must be taken into account are discussed in these Guidelines. An experimentally determined NOEL does not prove or disprove the existence of a threshold, although many developmental toxicologists assume a threshold for most developmental effects because of known repair capabilities in developing systems and the fact that many developmental alterations are multifactorial in nature.

51 FR 34042

GUIDELINES FOR ESTIMATING EXPOSURES

SUMMARY: On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for Estimating Exposures.

The Guidelines for Estimating Exposures (hereafter "Guidelines") are intended to guide Agency analysis of exposure assessment data in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for Exposure Assessment published November 23, 1984 (49 FR 46304).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

FOR FURTHER INFORMATION CONTACT:

Dr. Richard V. Moraski
Exposure Assessment Group
Office of Health and Environmental Assessment (RD-689)
U. S. Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460
202-475-8923

SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process.* In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for Estimating Exposures

Work on the Guidelines for Estimating Exposures began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the field of exposure assessment from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (49 FR 46304). On November 9, 1984, the Administrator directed that Agency offices use the proposed guidelines in performing risk assessments until final guidelines become available.

After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and preliminary Agency responses to those comments. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for Estimating Exposures were concurred on in a letter dated January 13, 1986. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The SAB requested that the Agency develop guidelines on the principles for the measurement of pollutant concentrations in the various environmental media and for the uses of environmental measurements for exposure assessment. This effort is currently underway.

The Agency also will provide technical support documents that contain detailed technical information needed to implement the Guidelines. Two of these technical reports entitled "Development of Statistical Distributions or Ranges of Standard Factors Used in Exposure Assessments" (available from the National Technical Information Service, PB85-242667) and "Methodology for Characterization of Uncertainty in Exposure Assessments" (available from the National Technical Information Service, PB85-240455) are currently available. Technical support documents will be revised periodically to reflect improvements in exposure assessment methods and new information or experience.

[51 FR 34043]

The Agency is continuing to study the risk assessment issues raised in the Guidelines and will revise these Guidelines in line with new information, as appropriate.

References, supporting documents, and comments received on the proposed guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

CONTENTS

Part A: Guidelines for Estimating Exposures

I. Introduction

These Guidelines provide the Agency with a general approach and framework for carrying out human or nonhuman exposure assessments for specified pollutants. The Guidelines have been developed to assist future assessment activities and encourage improvement in those EPA programs that require, or could benefit from, the use of exposure assessments. The Guidelines are procedural. They should be followed to the extent possible in instances where exposure assessment is a required element in the regulatory process or where exposure assessments are carried out on a discretionary basis by EPA management to support regulatory or programmatic decisions.

This document, by laying out a set of questions to be considered in carrying out an exposure assessment, should help avoid inadvertent mistakes of omission. Ideally, exposure assessments are based on measured data. EPA recognizes that gaps in data will be common, but the Guidelines will nevertheless serve to assist in organizing the data that are available, including new data developed as part of the exposure assessment. In the absence of sufficient reliable data and the time to obtain appropriate measurements, exposure assessments may be based on validated mathematical models. Whenever possible, exposure assessments based on modeling should be complemented by reliable measurements. Furthermore, it is understood that the level of detail found in the exposure assessments depends on the scope of the assessment.

These Guidelines should also promote consistency among various exposure assessment activities that are carried out by the Agency. Consistency with respect to common physical, chemical, and biological parameters, with respect to assumptions about typical exposure situations, and with respect to the characterization of uncertainty of estimates, will enhance the comparability of results and enable the Agency to improve the state-of-the-art of exposure assessment over time through the sharing of common data and experiences.

It is recognized that the main objective of an exposure assessment is to provide reliable data and/or estimates for a risk assessment. Since a risk assessment requires the coupling of exposure information and toxicity or effects information, the exposure assessment process should be coordinated with the toxicity/effects assessment. This document provides a common approach to format, which should simplify the process of reading and evaluating exposure assessments and thereby increase their utility in assessing risk.

As the Agency performs more exposure assessments, the Guidelines will be revised to reflect the benefit of experience.

II. General Guidelines and Principles

A. Exposure and Dose

Exposure has been defined by Committee E-47, Biological Effects and Environmental Fate, of the American Society for Testing and Materials, as the contact with a chemical or physical agent. The magnitude of the exposure is determined by measuring or estimating the amount of an agent available at the exchange boundaries, i.e., lungs, gut, skin, during some specified time. Exposure assessment is the determination or estimation (qualitative or quantitative) of the magnitude, frequency, duration, and route of exposure. Exposure assessments may consider past, present, and future exposures with varying techniques for each phase, e.g., modeling of future exposures, measurements of existing exposure, and biological accumulation for past exposures. Exposure assessments are generally combined with environmental and health effects data in performing risk assessments.

In considering the exposure of a subject to a chemical agent, there are several related processes. The contact between the subject of concern and the agent may lead to the intake of some of the agent. If absorption occurs, this constitutes an uptake (or an absorbed dose). When biological tissue or fluid measurements indicate the presence of a chemical, exposures may be estimated from these data. Presence of a chemical in such biological samples is the most direct indication that an exposure has occurred. The route of exposure generally impacts the extent of absorption and should be considered in performing risk assessments.

[51 FR 34044]

B. Decision Path to Determine Scope of the Assessment

The first step in preparing an exposure assessment should be the circumscription of the problem at hand to minimize effort by use of a narrowing process. A decision path that describes this process is shown in Figure 1. As illustrated in Figure 1, the preliminary assessment and the in-depth assessment are two major phases in this logic path.

[51 FR 34046]

The preliminary assessment phase should commence by considering what risk is under study. Within this framework, a data base should be compiled from readily available scientific data and exposure information based on manufacturer, processor, and user practices. Next, the most likely areas of exposure (manufacturing, processing, consumer, distribution, disposal, water and food, etc.) should be identified. The preliminary exposure assessments should be based on data derived from environmental measurements. When a limited amount of measurement data is available, estimates may be based on modeling. Since a complete data search may not be possible, well identified

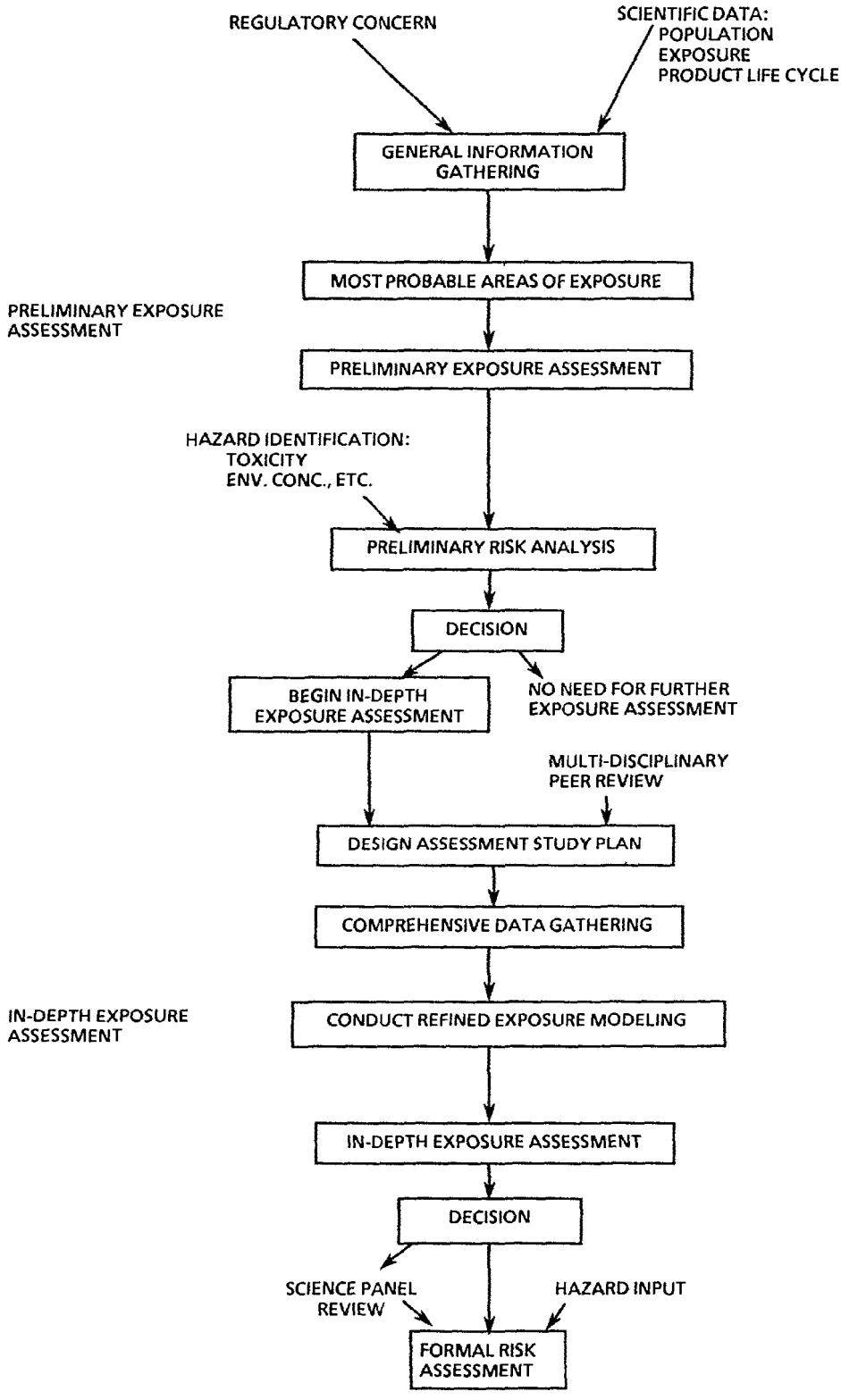

Figure 1. Decision path for exposure assessment.

assumptions and order of magnitude estimates may be used to further narrow the exposure areas of concern.

Data from this preliminary exposure assessment can then be coupled with toxicity information to perform a preliminary risk analysis. As a result of this analysis, a decision will be made that either an in-depth exposure assessment is necessary or that there is no need for further exposure information. The organization and contents of an in-depth exposure assessment are given in the following section.

In assembling the information base for either a preliminary assessment or a more detailed assessment, its adequacy should be ascertained by addressing the following considerations:

- Availability of information in every area needed for an adequate assessment;
- Quantitative and qualitative nature of the data;
- Reliability of information;
- Limitations on the ability to assess exposure.

C. Uncertainty

Exposure assessments are based on measurements, simulation model estimates, and assumptions about parameters used in approximating actual exposure conditions. Actual measurements should be used whenever possible. Both data and assumptions contain varying degrees of uncertainty which influence the accuracy of exposure assessments. Consequently, evaluation of uncertainty is an important part of all exposure assessments.

The uncertainty analyses performed will vary depending on the scope of the assessment, the quantity and quality of measurements, and the type and complexity of mathematical models used. A discussion of the types of analyses used for quantifying uncertainties in exposures is presented in the next section.

III. Organization and Contents of an Exposure Assessment

A. Overview

A suggested outline for an exposure assessment document is given in Exhibit 1. The five major topics to be addressed within most exposure assessments are as follows: Source(s), Exposure Pathways, Measured or Estimated Concentrations and Duration, Exposed Population(s), and Integrated Exposure Analysis. These five topics are appropriate for exposure assessments in general, whether the assessments are of global, national, regional, local, site specific, workplace related, or other scope. The topics are appropriate for exposure assessments on new or existing chemicals and radionuclides. They are also applicable to both single media and multimedia assessments. Since exposure assessments are performed at different levels of detail, the extent to which any assessment contains items listed in Exhibit 1 depends upon its scope. The outline is a guide to organize the data whenever they are available.

Exhibit 1.--Suggested Outline for an Exposure Assessment

1. Executive Summary
2. Introduction
   a. Purpose
   b. Scope
3. General Information for Each Chemical or Mixture
   a. Identity
      (1) Molecular formula and structure, synonyms, and Chemical Abstracts Service (CAS) number
      (2) Description of grades, contaminants, and additives
      (3) Other identifying characteristics
   b. Chemical and Physical Properties
4. Sources
   a. Characterization of Production and Distribution
   b. Uses
   c. Disposal
   d. Summary of Environmental Releases
5. Exposure Pathways and Environmental Fate
   a. Transport and Transformation
   b. Identification of Principal Pathways of Exposure
   c. Predicting Environmental Distribution
6. Measured or Estimated Concentrations
   a. Uses of Measurements
   b. Estimation of Environmental Concentrations
7. Exposed Populations
   a. Human Populations
      (1) Population size and characteristics
      (2) Population location
      (3) Population habits
   b. Nonhuman Populations (where appropriate)
      (1) Population size and characteristics
      (2) Population location
      (3) Population habits
8. Integrated Exposure Analysis
   a. Calculation of Exposure
      (1) Identification of the exposed population and critical elements of the ecosystem
      (2) Identification of pathways of exposure
   b. Human Dosimetry and Biological Measurements
   c. Development of Exposure Scenarios and Profiles
   d. Evaluation of Uncertainty
      (1) Introduction
      (2) Assessments based on limited initial data
      (3) Assessments based on subjective estimates of input variable distributions
      (4) Assessments based on data for model input variables
      (5) Assessments based on data for exposure
      (6) Summary
9. References
10. Appendices

B. Detailed Explanation of Outline

1. Executive Summary. The "Executive Summary" should be written so that it can stand on its own as a miniature report. Its main focus should be on a succinct description of the procedures used, assumptions employed, and summary tables or charts of the results. A brief discussion of the uncertainties associated with the results should be included.

2. Introduction (Purpose and Scope). This section should state the intended purpose of the exposure assessment and identify the agent being

investigated, the types of sources and exposure routes included, and the populations of concern.

3. General Information for Each Chemical or Mixture.

a. Identity.

(1) Molecular formula and structure, synonyms, and Chemical Abstracts Service number.

(2) Description of grades, contaminants, and additives.

(3) Other identifying characteristics.

b. Chemical and Physical Properties. This subsection should provide a summary description of the chemical and physical properties of the agent. Particular attention should be paid to the features that would affect its behavior in the environment.

4. Sources. The points at which a substance is believed to enter the environment should be described, along with any known rates of entry. (Points of entry may be indoors as well as outdoors; environments include indoor settings such as offices as well as outdoor environments.) A detailed exposure assessment should include a study of sources, production, uses, destruction/disposal, and environmental release of a substance. The studies

[51 FR 34047]

should include a description of human activities with respect to the substance and the environmental releases resulting from those activities. It should account for the controlled mass flow of the substance from creation to destruction and provide estimates of environmental releases at each step in this flow. Seasonal variations in environmental releases should also be examined. All sources of the substance should be accounted for with the sum of the uses, destruction, and the environmental releases. The environmental releases can be described in terms of geographic and temporal distribution and the receiving environmental media, with the form identified at the various release points.

a.Characterization of Production and Distribution. All sources of the substance's release to the environment, consistent with the scope of the assessment, should be included, such as production, extraction, processing, imports, stockpiles, transportation, accidental/ incidental production as a side reaction, and natural sources. The sources should be located, and activities involving exposure to the substance should be identified.

b. Uses. The substance should be traced from its sources through various uses (with further follow-up on the products made to determine the presence of the original material as an impurity), e.g., exports, stockpile increases, etc.

c. Disposal. This subsection should contain an evaluation of disposal sites and destruction processes, such as incineration of industrial chemical waste, incineration of the substance as part of an end-use item in municipal waste, landfilling of wastes, biological destruction, or destruction in the process of using the end product. Hazardous contaminants of the substance may be included, and products containing the substance as a contaminant may be followed from production through destruction/disposal.

d. Summary of Environmental Releases. Estimates should be made of the quantities of the substance released to the various environmental media. Sources of release to the environment include production, use, distribution/transport, natural sources, disposal, and contamination of other products. Environmental releases should be presented at a reasonable level of detail. Extremely detailed exposure estimates would attempt to specify the following information for each significant emission source: location, amount of the substance being released as a function of time to each environmental medium, physical characteristics of the emission source, and the physical and chemical form of the substance being released. Evaluation of the uncertainties associated with the emission estimates should be given. A detailed discussion of the procedures for estimating uncertainty is presented in section 8.d.

5. Exposure Pathways and Environmental Fate. The exposure pathways section should address how an agent moves from the source to the exposed population or subject. For a less detailed assessment, broad generalizations on environmental pathways and fate may be made. In the absence of data, e.g., for new substances, fate estimates may have to be predicted by analogy with data from other substances. Fate estimates may also be made by using measurements and/or models and laboratory-derived process rate coefficients. At any level of detail, certain pathways may be judged insignificant and not pursued further.

For more detailed assessments involving environmental fate, the analysis of sources described previously should provide the amount and rate of emissions to the environment, and possibly the locations and form of the emissions. The environmental pathways and fate analysis follows the substance from its point of initial environmental release, through the environment, to its ultimate fate. It may result in an estimation of the geographic and temporal distribution of concentrations of the substance in the various contaminated environmental media.

a. Transport and Transformation. The substance, once released to the environment, may be transported (e.g., convected downstream in water or on suspended sediment, through the atmosphere, etc.) or physically transformed (e.g., volatilized, melted, absorbed/desorbed, etc.); may undergo chemical transformation, such as photolysis, hydrolysis, oxidation, and reduction; may undergo biotransformation, such as biodegradation; or may accumulate in one or more media. Thus, the environmental behavior of a substance should be

evaluated before exposures are assessed. Factors that should be addressed include:

- How does the agent behave in air, water, soil, and biological media? Does it bioaccumulate or biodegrade? Is it absorbed or taken up by plants?
- What are the principal mechanisms for change or removal in each of the environmental media?
- Does the agent react with other compounds in the environment?
- Is there intermedia transfer? What are the mechanisms for intermedia transfer? What are the rates of the intermedia transfer or reaction mechanisms?
- How long might the agent remain in each environmental medium? How does its concentration change with time in each medium?
- What are the products into which the agent might degrade or change in the environment? Are any of these degradation products ecologically or biologically harmful? What is the environmental behavior of the harmful products?
- Is a steady-state concentration distribution in the environment, or in specific segments of the environment, achieved? If not, can the nonsteady-state distribution be described?
- What is the resultant distribution in the environment--for different media, different types or forms of the agent, for different geographical areas, at different times or seasons?

b. Identification of Principal Pathways of Exposure. The principal pathway analysis should evaluate the sources, locations, and types of environmental releases, together with environmental behavioral factors, to determine the significant routes of human and environmental exposure to the substance. Thus, by listing the important characteristics of the environmental release (entering media, emission rates, etc.) and the agent's behavior (intermedia transfer, persistence, etc.) after release to each of the entering media, it should be possible to follow the movement of the agent from its initial release to its subsequent fate in the environment. At any point in the environment, human or environmental exposure may occur. Pathways that result in major concentrations of the agent and high potential for human or environmental contact are the principal exposure pathways.

c. Predicting Environmental Distribution. Models may be used to predict environmental distributions of chemicals. Model estimates of environmental distribution of chemicals are based on measurements whenever feasible. In predicting environmental distributions of chemicals, available measurements must be considered.

In this section an estimation is made, using appropriate models, of representative concentrations of the agent in different environmental media, and its time-dependence in specific geographical locations (e.g., river basins, streams, etc.).

6. Measured or Estimated Concentrations.

a. Uses of Measurements. Measurements are used to identify releases (source terms) and, in the

[51 FR 34048]

exposure pathways and fate assessments, to quantitatively estimate both release rates and environmental concentrations. Some examples of uses of measurements are: sampling of stacks or discharge pipes for emissions to the environment, testing of products for chemical or radionuclide content, testing of products for chemical or radioactive releases, sampling of appropriate points within a manufacturing plant to determine releases from industrial processes or practices, sampling of potentially exposed populations using personal dosimeters, and sampling of solid waste for chemical or radionuclide content. These data should be characterized as to accuracy, precision, and representativeness. If actual environmental measurements are unavailable, concentrations can be estimated by various means, including the use of fate models (see previous section) or, in the case of new chemicals, by analogy with existing chemicals.

Measurements are a direct source of information for exposure analysis. Furthermore, reliable measurements can be used to calibrate or extrapolate models or calculations to assess environmental distributions. However, environmental pathway and fate analysis may be needed in addition to the measured data for the following reasons: for most pollutants, particularly organic and new chemicals, measurements are limited; analysis of measured data does not often yield relationships between environmental releases and environmental concentration distribution in media or geographic locations that have not been measured; analysis of measurements does not provide information on how and where biota influence the environmental distribution of a pollutant; and measured concentrations may not be traceable to individual sources.

b. Estimation of Environmental Concentrations. Concentrations of agents should be estimated for all environmental media that might contribute to significant exposures. Generally, the environmental concentrations are estimated from measurements, mathematical models, or a combination of the two. If environmental measurements are not limited by sample size or inaccuracies, then exposure assessments based on measurements have precedence over estimates based on models.

The concentrations must be estimated and presented in a format consistent with available dose-response information. In some cases an estimate of annual average concentration will be sufficient, while in other cases the temporal distribution of concentrations may be required. Future environmental concentrations resulting from current or past releases may also be projected. In some cases, both the temporal and geographic distributions of the concentration may be assessed.

Moreover, if the agent has natural sources, the contribution of these to environmental concentrations may be relevant. These "background" concentrations may be particularly important when the results of tests of toxic effects show a threshold or distinctly nonlinear dose-response.

The uncertainties associated with the estimated concentrations should be evaluated by an analysis of the uncertainties of the model parameters and input variables. When the estimates of the environmental concentrations are based on mathematical models, the model results must be compared to available measurements, and any significant discrepancies should be discussed. Reliable, analytically-determined values must be given precedence over estimated values whenever significant discrepancies are found.

7. Exposed Populations. Populations selected for study may be done *a priori*, but frequently the populations will be identified as a result of the sources and fate studies. From an analysis of the distribution of the agent, populations and subpopulations (i.e., collections of subjects) at potentially high exposure can be identified, which will then form the basis for the populations studied. Subpopulations of high sensitivity, such as pregnant women, infants, chronically ill, etc., may be studied separately.

Census and other survey data may be used to identify and describe the population exposed to various contaminated environmental media. Depending on the characteristics of available toxicological data, it may be appropriate to describe the exposed population by other characteristics such as species, subspecies-age-sex distribution, and health status.

In many cases, exposed populations can be described only generally. In some cases, however, more specific information may be available on matters such as the following:

a. Human Populations

(1) Population size and characteristics (e.g., trends, sex/age distribution)

(2) Population location

(3) Population habits-- transportation habits, eating habits, recreational habits, workplace habits, product use habits, etc.

b. Nonhuman Populations (where appropriate)

(1) Population size and characteristics (e.g., species, trends)

(2) Population location

(3) Population habits

8. Integrated Exposure Analysis. The integrated exposure analysis combines the estimation of environmental concentrations (sources and fate information) with the description of the exposed population to yield exposure profiles. Data should be provided on the size of the exposed populations; duration, frequency, and intensity of exposure; and routes of exposure. Exposures should be related to sources.

For more detailed assessments, the estimated environmental concentrations should be considered in conjunction with the geographic distribution of the human and environmental populations. The behavioral and biological characteristics of the exposed populations should be considered, and the exposures of populations to various concentration profiles should be estimated. The results can be presented in tabular or graphic form, and an estimate of the uncertainty associated with them should be provided.

a. Calculation of Exposure. The calculation of exposure involves two major aspects:

(1) Identification of the exposed population and critical elements of the ecosystem.

The estimate of environmental concentrations also should give the geographical areas and environmental media contaminated. The stated purpose of the assessment should have described the human and environmental subjects for which exposures are to be calculated. If the subjects are not listed, the contaminated geographical areas and environmental media can be evaluated to determine subject populations. The degree of detail to be used in defining the exposed population distribution depends on the concentration gradient over geographic areas.

(2) Identification of pathways of exposure.

(a) Identification and description of the routes by which the substances travel from production site, through uses, through environmental releases/sources, through transport and fate processes, to the target population.

(b) Quantitative estimates of the amounts of the chemical following each exposure pathway. Such estimates allow the various pathways to be put in the perspective of relative importance.

From the geographic and temporal distribution of environmental

[51 FR 34049]

concentrations, the exposed population, the behavioral characteristics, and the critical elements of the ecosystem, exposure distributions can be estimated. The results of exposure calculation should be presented in a format that is consistent with the requirements of the dose-response functions which may later be used in a risk assessment. For example, when health risks caused by exposure over extended durations are considered, average daily exposure over the duration of exposure usually is calculated. When lifetime risks are considered, average daily exposure over a lifetime usually is calculated. In contrast, when health risks caused by exposures over short durations are considered, exposure rates are calculated over short time intervals to ensure that peak risks are defined. Many exposure assessments are based on the average exposure occurring over the exposure period. The range of possible exposures is usually divided into intervals,

and the exposures within each interval are counted. The results can be presented in tabular form or as a histogram.

The population residing in a specific geographic area may be exposed to a substance from several exposure routes. For each exposure route, exposure of individuals in these populations may be determined by summing the contribution of all sources to the exposure route. When exposures involve more than one exposure route, the relative amounts of a substance absorbed is usually route dependent. Consequently, total absorbed dose estimates must account for these differences. Because EPA regulates sources of releases, the contribution to exposures from each type of source being considered should be displayed. Exposure estimates should be presented for each significant exposure route, and the results should be tabulated in such a way that total externally applied and absorbed dose can be determined.

b. Human Dosimetry and Biological Measurements. Biological measurements of human body fluids and tissues for substances or their metabolites can be used to estimate current or past exposure to chemicals. When analytical methods are available, chemicals that have been absorbed into the body can be measured in body tissue and fluid. Such measurements may be used to estimate human exposure if the chemical substances leave in the body reliable indicators of exposure. Furthermore, although a compound may be relatively easy to detect in body tissue, for some compounds, attributing body burdens to specific environmental releases may be difficult because of limited ability to obtain environmental measurements or appropriate metabolic data.

c. Development of Exposure Scenarios and Profiles. Depending on the scope of the exposure assessment, the total exposure may be fractionated into one or more "exposure scenarios" to facilitate quantification. As an example, Table 1 lists seven very broad scenarios: Occupational, Consumer, Transportation, Disposal, Food, Drinking Water, and Ambient. For each of the scenarios, the major topics necessary to quantify exposure include sources, pathways, measurements, and population characteristics. Investigation of only one scenario may be necessary for the scope of some assessments. For example, a pesticide application exposure assessment may consider the occupational scenario which would address the exposure to applicators and populations in the vicinity of the site. An exposure assessment around a hazardous waste site may focus on the disposal scenario. The exposure assessment

TABLE 1.--EXPOSURE ASSESSMENT INFORMATION NEEDS FOR VARIOUS EXPOSURE SCENARIOS

Exposure scenario	Sources	Fate	Population Characteristics	Measurement
Occupational (chemical production).	Site/plant locations, in-plant/on-site materials balance.	Physical and chemical properties models.	Workers, families, population around sites/plants.	In-plant/on-site releases, ambient levels surrounding site/plants; human dosimetry.
Consumer (direct use of chemical or inadvertent use).	Consumption rates, distribution pattern amounts in products.	Physical and chemical properties, shelf life release rates, models.	Consumers	Levels in products releases.
Transportation / storage/spills.	Patterns of distribution and transportation; models for spills.	Physical and chemical properties, environmental fate models.	Storage, transportation workers, general population in area.	Releases, ambient levels.
Disposal (include incineration, landfill).	Materials balance around disposal method, efficiency,releases to environment.	Fate within disposal process; environmental fate of releases; models.	Workers at site of disposal, general population around site.	Releases, levels at various points within process, ambient levels.
Food	Food chain, packaging, additives.	Food chain models, fate during preparation or processing of food.	General population, nonhuman population.	Levels in food, feedstuff; food chain sampling.
Drinking water	Groundwater, surface water, distribution system.	Leach rates from pipes, chlorination processes, fate in water; models.	General population.	Levels in drinking water, groundwater, surface water, treatment plants.
Ambient	Releases to environment; air, land, water.	Environmental fate models.	General population, nonhuman population.	Ambient air, water, soil, etc.; human dosimetry.

also may consider other scenarios. The more extensive and comprehensive the scope, the more scenarios are usually involved.

It will usually be advantageous in performing an exposure assessment to identify exposure scenarios, quantify the exposure in each scenario, and then integrate the scenarios to estimate total exposure. In this "integrated exposure analysis," the summation of independent exposures from different scenarios (keeping exposure routes separate) often will result in a breakout of exposure by subpopulations, since the individual scenarios usually treat exposure by subpopulation. Therefore, the integration of the scenarios, or integrated exposure analysis, will often result in an exposure profile.

For each exposed subpopulation, exposure profiles should include the size of the group, the make-up of the group (age, sex, etc.), the source of the agent, the exposure pathways, the frequency and the intensity of exposure by each route (dermal, inhalation, etc.), the duration of exposure, and the form of the agent when exposure occurs. Assumptions and uncertainties associated with each scenario and profile should be clearly discussed.

d. Evaluation of Uncertainty.

(1) Introduction. Often an exposure assessment progresses through several stages of refinement. The purpose of these Guidelines is to present methods appropriate for characterization of uncertainty for assessments at various stages of refinement, from assessments based on limited initial data to those based on extensive data.

The appropriate method for characterizing uncertainty for an exposure assessment depends upon the underlying parameters being estimated, the type and extent of data available, and the estimation procedures utilized.

[51 FR 34050]

The uncertainty of interest is always with regard to the population characteristic being estimated. For example, when the population distribution of exposures is being estimated, characterization of uncertainty addresses the possible differences between the estimated distribution of exposure and the true population distribution of exposure.

An exposure assessment quantifies contact of a substance with affected population members (human or nonhuman subjects). The measure of contact (e.g., environmental level or absorbed dose) depends upon what is needed to predict risk. An integrated exposure assessment quantifies this contact via all routes of exposure (inhalation, ingestion, and dermal) and all exposure pathways (e.g., occupational exposure, exposure from consumption of manufactured goods, etc.). The exposed population generally is partitioned into subpopulations such that the likely exposure of all members of a subpopulation is attributable to the same sources. The exposure for each member of a subpopulation is then the sum of exposures over a fixed set of sources and pathways. The measured or estimated exposures for members of a subpopulation are ideally used to estimate the subpopulation distribution of exposure or characteristics thereof. However, a lack of sufficient information sometimes precludes estimation of the subpopulation distributions of exposure and only summary measures of this distribution, such as the mean, minimum, maximum, etc., are estimated. In each case, characterization of uncertainty for the exposure assessment primarily addresses limitations of the data and the estimation procedures. The proportions of the population members in the individual subpopulations are usually estimated and can be used (by combining estimated distributions for the subpopulations) to estimate the distribution of exposure for the total population. Uncertainty concerning the sizes of the subpopulations should be addressed by discussing limitations of the data and estimation methods as well as by tabulating confidence interval estimates for the population sizes whenever possible.

(2) Assessments based on limited initial data. The initial exposure assessment for a substance may be based on limited data for exposure and/or input variables for an exposure prediction model (i.e., an equation that expresses exposure as a function of one or more input variables). These data might be either extant data or data produced by an initial small-scale study. The limited initial data frequently are insufficient to permit estimation of the entire distribution of exposure. Instead, summary measures of this distribution, such as the mean, minimum, and maximum, are usually estimated.

If the assessment is based on measured exposures, the methods used to characterize uncertainty depend mainly upon whether or not the data result from a probability sample for which the probability of inclusion is known for each sample member. Characterization of uncertainty for an assessment based on a probability sample of exposures is discussed later in section 8.d.(5). If the measured exposures are not based on a probability sample, acknowledgement that no strictly valid statistical inferences can be made beyond the units actually in the sample is one aspect of the characterization of uncertainty. If inference procedures are implemented, the assumptions upon which these inferences are based (e.g., treatment of the sample as if it were a simple random sample, or assumption of an underlying model) should be explicitly stated and justified. The data collection methods and inherent limitations of the data should also be discussed.

An initial exposure assessment also may be based on limited data, such as estimated ranges, for input variables for an exposure prediction model. The exposure prediction model would be derived from a postulated exposure scenario that describes the pathways from sources to contact with population members. If the data were only sufficient to support estimates of the ranges of the input variables, the exposure assessment might be limited

to a sensitivity analysis. The purpose of the sensitivity analysis would be to identify influential model input variables and develop bounds on the distribution of exposure. A sensitivity analysis would estimate the range of exposures that would result as individual model input variables were varied from their minumum to their maximum possible values with the other input variables held at fixed values, e.g., their midranges. The overall minimum and maximum possible exposures usually would be estimated also. For an exposure assessment of this type, the uncertainty would be characterized by describing the limitations of the data used to estimate possible ranges of model input variables and by discussing justification for the model. Justification of the model should include a description of the exposure scenario, choice of model input variables, and the functional form of the model. Sensitivity to the model formulation also can be investigated by replicating the sensitivity analysis for plausible alternative models.

The sensitivity analysis can be enhanced by computing the predicted exposures that result from all possible input variable combinations. If each input variable has only a finite set of possible values, the set of all possible combinations of the input variables can be formed, and the predicted exposure can be computed for each combination. These exposure predictions can be used to form a distribution of exposures by counting the number of occurrences at each exposure level or interval of exposures. This is equivalent to estimating the distribution of exposures that results from treating all input variable combinations as equally likely. This procedure can also be applied by transforming continuous input variables into discrete ones and representing them by equally spaced points. In the limit, as the equal spaces become small and the number of points becomes large, the distribution of exposure that results from counting occurrences of exposure levels is equivalent to estimating the distribution of exposures that results from statistically independent, continuous input variables with uniform distributions on the estimated ranges. This estimated distribution of exposure values can be produced by Monte Carlo simulation, one of the methods of mathematical statistics. The Monte Carlo method consists of randomly generating input variate values and using these to compute corresponding exposure levels, generating an exposure distribution via many iterations. Interpretation of statistics based on this exposure distribution would be in terms of the equally likely input variable combinations. For example, the 95th percentile of this distribution would be the exposure level exceeded by only 5% of the exposures resulting from treating all combinations of input variable values as equally likely. Although this distribution of exposures cannot be interpreted as an estimate of the population distribution (unless the input variables actually are statistically independent and uniformly distributed), it provides additional information for making regulatory decisions. Characterization of uncertainty would include a discussion of limitations of the data and justification for the model as discussed above. Sensitivity to model formulation could also be investigated by estimating the distribution of exposure that results from using the

[51 FR 34051]

same uniform input variable distributions with plausible alternative models and comparing the estimated percentiles.

(3) Assessments based on subjective estimates of input variable distributions. If a model has been formulated that expresses exposure as a function of one or more input variables, the methods of mathematical statistics, such as Monte Carlo simulation, can be used to estimate the population distribution of exposure from an estimate of the joint distribution of the model input variables. Ideally, model input variables should be represented by empirically-validated probability distributions. In some cases, it may be possible to formulate an estimate of the joint distribution of model input variables from discussions with subject matter experts (e.g., via histograms for statistically-independent input variables). The estimated population distribution of exposure will be equivalent to the distribution discussed in section 8.d.(2) for equally likely combinations of input variable values only when the input variable distributions supported are independent uniform distributions. When qualitative knowledge of input variable distributions is used to estimate the population distribution of exposure, uncertainty is characterized by discussing justification for the presumed model and input variable distributions. Alternative models and/or alternative input variable distributions also should be discussed. Sensitivity to these alternatives can be investigated by estimating the distributions of exposure that result from plausible alternatives and comparing the percentiles of the estimated exposure distributions. All available data, even if data are limited, should be used to validate the presumed input variable distributions and the predicted distribution of exposure.

(4) Assessments based on data for model input variables. The exposure assessment based on an estimate of the joint probability distribution for model input variables can be refined by collecting sample survey data for model input variables for a sample of population members. The population distribution of exposure can then be estimated by computing the expected exposure for each sample member based on the model. These expected exposures can be used to directly compute confidence interval estimates for percentiles of the exposure distribution. Alternatively, the sample survey data can be used to compute joint confidence interval estimates for percentiles of the input variable

distribution, which can then be used to generate confidence interval estimates for percentiles of the exposure distribution. In either case, the interval estimates for percentiles of the exposure distribution are a useful quantitative characterization of uncertainty.

Characterization of uncertainty for the exposure assessment would contain a thorough discussion of limitations of the data and justification for the model used to compute expected exposures. The design of the sample survey used to produce the data base should also be discussed. If a probability sample were not used, the lack of a probability sample would be an additional source of uncertainty. Any assumptions used in computing the confidence interval estimates, such as independence of model input variables, should be explicitly stated and justified. Sensitivity to model formulation can be investigated by estimating the distribution of exposure for plausible alternative models and comparing the estimated percentiles, if sample survey data have been collected for the input variables of the alternative models. Appropriate available data for exposure should be used to validate the predicted distribution of exposure. If specific probability distributions have been presumed for any model input variables, the data for these variables should be used to test for goodness of fit for these distributions.

(5) Assessments based on data for exposure. A major reduction in the uncertainty associated with an exposure assessment can be achieved by directly measuring the exposure for a sufficiently large sample of members of the affected population. This reduction in uncertainty is achieved by eliminating the use of a model to predict exposure. The measured exposure levels can be used to directly estimate the population distribution of exposure and confidence interval estimates for percentiles of the exposure distribution. Direct confidence interval estimates also can be computed for other characteristics of the exposure distribution, such as the mean exposure.

These confidence interval estimates are then the primary characterization of uncertainty for the exposure assessment. Limitations of the data and design of the sample survey used to collect the data also should be discussed. If the sample was not a probability sample, this would again be an additional source of uncertainty.

(6) Summary. A summary of the primary methods recommended for characterizing uncertainty in exposure assessments is presented in Table 2. Virtually all exposure assessments, except those based on measured exposure levels for a probability sample of population members, rely upon a model to predict exposure. The model may be any mathematical function, simple or complex, that expresses an individual's exposure as a function of one or more input variables. Whenever a model that has not been validated is used as the basis for an exposure assessment, the uncertainty associated with the exposure assessment may be substantial. The primary characterization of uncertainty is at least partly qualitative in this case, i.e., it includes a description of the assumptions inherent in the model and their justification. Plausible alternative models should be discussed. Sensitivity of the exposure assessment to model formulation can be investigated by replicating the assessment for plausible alternative models.

[51 FR 34052]

When an exposure assessment is based on directly measured exposure levels for a probability sample of population members, uncertainty can be greatly reduced and described quantitatively. In this case, the primary sources of uncertainty are measurement errors and sampling errors. The effects of these sources of error are measured quantitatively by confidence interval estimates of percentiles of the exposure distribution. Moreover, the sampling errors can be limited by taking a large sample.

Whenever it is not feasible to take a large sample, it is sometimes possible to obtain at least some data for exposure and model input variables. These data should be used to assess goodness of fit of the model and/or presumed distributions of input variables. This substantially reduces the amount of quantitative uncertainty for estimation of the distribution of exposure and is strongly recommended. It is recognized, however, that it may not be feasible to collect such data.

9.References. The references should contain a listing of all reports, documents, articles, memoranda, contacts, etc. that have been cited in the report.

10.Appendices. The appendices may contain such items as memoranda and letters that are not readily accessible, other tables of measurements, detailed lists of emission sources, detailed tables of exposures, process flow diagrams, mathematical model formulations, or any other item that may be needed to describe or document the exposure assessment.

Part B: Response to Public and Science Advisory Board Comments

I. Introduction

This section summarizes some of the issues raised in public comments on the Proposed Guidelines for Exposure Assessment published November 23, 1984 (49 FR 46304). Comments were received from 29 individuals or organizations. The Agency's initial summary of comments was presented to the Exposure Assessment Guidelines Review Group of the Science Advisory Board (SAB) on March 4, 1985. At its April 22-23, 1985, meeting, the panel provided the Agency with suggestions and recommendations concerning the Guidelines.

The SAB and public commentors expressed diverse opinions and addressed issues from a variety of perspectives. While most commentors supported the Guidelines, two urged withdrawal of the

TABLE 2.--SUMMARY OF PRIMARY METHODS FOR CHARACTERIZING UNCERTAINTY FOR ESTIMATING EXPOSURES

Type and extent of data	Population characteristic being estimated	Primary methods for characterizing uncertainty	
		Qualitative methods	Quantitative methods
Measured exposures for a large sample of population members.	Distribution of exposure.	1. Limitations of the survey design and measurement techniques.	1. Confidence interval estimates for percentiles of the exposure distribution. 2. Goodness of fit for exposure models, if any have been postulated.
Measured exposures for a small sample of population members.	Summary parameter(s) of the exposure distribution, e.g., mean or a percentile.	1. Limitations of the survey design and. measurement techniques.	1. Confidence interval estimate for the summary parameter(s). 2. Goodness of fit for exposure models,. if any have been postulated.
Measured model input variables for a large sample of population members.	Distribution of exposure.	1. Limitations of the survey.design and measurement techniques. 2. Validity of the exposure model.	1. Confidence interval estimates for percentiles of the exposure distribution. 2. Goodness of fit for input variable distribution functions, if any have been postulated. 3. Estimated distribution of exposure based on alternative models.
Estimated distributions of model input variables.	Distribution of exposure.	1. Validity of the exposure model. 2. Limitations of the data. or other basis for the input variable distributions.	1. Confidence interval estimates for percentiles of the exposure distribution. 2. Goodness of fit for input variable distributions, if input variable data are available. 3. Estimated distribution of exposure based on alternative models.
Limited data for model input variables.	Minimum, maximum, and range of the exposure distribution.	1. Limitations of the data. 2. Validity of the exposure model.	If input variable data are very limited, e.g., some extant data collected for other purposes, quantitative characterization of uncertainty may not be possible.

document. The SAB Panel recommended that supplementary guidelines be written on the use of measurements in preparing exposure assessments. In addition, the Panel wished to see a greater emphasis in the current Guidelines on the use of measured data rather than models in generating exposure assessments. The Panel recommended that the technical support document entitled "Methodology for Characterization of Uncertainty in Exposure Assessments" be expanded with additional examples.

In response to the comments, the Agency has modified or clarified many sections of the Guidelines, and is planning to develop supplementary guidance in line with the SAB recommendations. The discussion that follows highlights significant issues raised in the comments, and the Agency's response to them. Also, many minor recommendations, which do not warrant discussion here, were adopted by the Agency.

II. General Information

A. Acceptable Latitude of Approach

Some commentors believe the Guidelines are too general and allow too much latitude in choice of approach and do not assure that "all" data, sources, limitations, etc. are considered before an exposure assessment is conducted. Others suggested that the Agency specify models to be used while others thought that only measured data should be allowed.

The Guidelines were developed to provide assistance in carrying out exposure assessments. The approach suggested is deliberately general in order to accommodate the development of exposure assessments with different levels of detail depending on the scope of the assessment. The Agency does not agree with the inclusion of such restrictive terminology as "in all cases." We cannot foresee all possible cases. We believe reasonable flexibility is a necessary ingredient for the proper implementation of the Guidelines while relying on uncertainty and sensitivity analyses to put the quality of the approach in perspective.

B. Technical Nature of Guidelines

Some commentors believe the language of the document is too technical for the lay person to understand; one commentor expressed misgivings concerning the "state-of-the-art" methods available for conducting exposure assessments.

While the Agency recognizes that the public has an interest in the Guidelines and invites comments from the public, the Guidelines are intended for use by technical/professional people. Providing guidelines written in lay terms would result in insufficient technical specifications to the professionals in the development of scientifically acceptable exposure assessments.

The Agency believes that the suggested procedures and methods in the Guidelines are commonly accepted. The Guidelines do not suggest the use of ad hoc, untested, and unvalidated procedures, but stress the use of the best scientific methods available with maximum analysis of existing data. This is both a scientific and practical approach that reflects the level of consensus within the Agency.

[51 FR 34053]

C. Measurements vs. Modeling

Some commentors support the use of measurements alone to develop an exposure assessment. Some believed there should be no data restraints; others thought all data should be validated. Other commentors argued for the use of simulation model estimates without measurements. One commentor objected to the use of unvalidated models to perform exposure assessments. In its review, the SAB strongly encouraged the Agency to develop a supplement to the current Guidelines on the development and use of measurements for exposure assessments.

The Agency encourages the use of validated measurements when available. The Guidelines specifically state that "Reliable, analytically determined values should be given precedence over estimated values. . ." and analytically determined values ". . .can be used to calibrate. . . models. . .to assess environmental distribution." Furthermore, in practice, exposure assessments performed by the Agency use published models with varying degrees of testing and validation. It is our belief that transport process models have been adequately validated over many years in most cases.

Furthermore, the Agency has revised the Guidelines to reflect the SAB suggestions that exposure assessments based on reliable measured data are preferred over model estimates whenever feasible.

III. Data Availability and Uncertainty Analysis

A. Information Uses

Some commentors asked for guidance in the use of information that may be false and how to deal with the potential situation when different models give different results. Others asked for model selection criteria.

The Guidelines clearly state the considerations that need to be addressed when assembling information bases for exposure assessments. Two considerations are: qualitative and quantitative nature of the data and the reliability of the information. Whether the exposure assessment is based on measurements or simulation model estimates, an evaluation of uncertainties associated with the data including source data and assumptions is necessary and important.

When there is uncertainty in the scientific facts, it is Agency policy to err on the side of public safety. The Agency intends to be realistic, but will not arbitrarily select midranges of environmental distributions that may compromise human health. In addition, quality assurance is an important matter that requires detailed attention. The collection of measured data and the development of methods to collect measurements are done by another office within the EPA. These issues will be handled by the Office of Acid Deposition, Environmental Monitoring, and Quality Assurance as they develop the supplemental guidelines for measurement of exposure.

Substantial work is currently being done on the development of mathematical model selection criteria. Results of these efforts will be published as a technical support document containing detailed information to further implement the Guidelines.

B. Worst-Case Estimates

A few commentors were concerned that worst-case estimates would be used when data are nonexistent or limited. The Guidelines do not encourage the use of worst-case assessments, but rather the development of realistic assessments based on the best data available.

A technical support document and a substantial section of the Guidelines currently discuss evaluation of uncertainty in order to produce objective assessments using the best (not worst-case) estimates available either for preliminary or in-depth exposure assessments. However, the Agency will err on the side of public health when evaluating uncertainties when data are limited or nonexistent.

IV. Evaluation of Uncertainties

A. Uncertainty Analysis

Many commentors felt that the sections of the Guidelines that dealt with uncertainty needed amplification while some sections as written were confusing. Some urged that uncertainty evaluation be presented and documented for each section within a specific exposure scenario in order to judge the overall plausibility of the assessment in reaching regulatory decisions.

Since the accuracy of an exposure assessment is influenced by the degrees of uncertainty contained in both data and assumptions, the Guidelines call for the evaluation of these uncertainties. The technical support document, Methodology for

Characterization of Uncertainty in Exposure Assessments (available from the National Technical Information Service, PB85-240455), describes in detail how such analyses can be performed. The Guidelines suggest that the uncertainty characterization include a discussion of the limitations of the data and estimation procedures as the justification for the model chosen. A sensitivity analysis of the exposure assessment is appropriate if the data were only able to support the estimates of ranges of the input variables. By identifying model input variables that determine the bounds on the distribution of exposure, the range of exposure, which results as individual model input variables are varied from minimum to maximum possible values as other variables remain constant, constitutes the sensitivity analysis. Further sensitivity of model formulation can be examined by repeating the sensitivity analysis for plausible alternative models.

Nothing in the Guidelines precludes estimation of uncertainty for each specific exposure scenario. The Agency has encouraged the evaluation of uncertainty in each aspect of the exposure assessment, which could impact the total risk estimate. It is important to estimate the level of uncertainty in risk assessments so that decisions based on risk assessment will reflect total uncertainty. The information presented in the Guidelines or the technical support documents properly and adequately describes the extent and quality of appropriate uncertainty analysis. Recognizing that the basis for the decision to refine a preliminary exposure assessment involves risk management, the Agency, at the suggestion of many commentors, decided to strike from the Guidelines the paragraph beginning "If the maximum possible exposure. . . ." in section III.B.8.d.(2).

B. Population Characterization

The Guidelines state that identification of populations and subpopulations at potentially high exposure forms the basis of the populations to be studied. Separate studies of sensitive subpopulation can also be included. Population characteristics, such as age and/or sex distributions, can be derived from the use of geographic and activity-specific data. Uncertainty related to estimation of a population characteristic include a discussion of the data limitations and the estimation procedures. In addition, uncertainty in estimating sizes of sensitive subpopulations should include estimates of confidence intervals.

Some commentors suggested the inclusion of additional characteristics, such as occupational and life style factors, and the inclusion of additional guidance concerning potential pitfalls when conducting population exposure

assessments. Others expressed concern that the exposure of a particular subpopulation would be combined with other exposures to produce an average exposure level for the general population.

The section describing population characterization encompasses, in general terms, the many characteristics that may be available, including life style factors, to describe exposed populations. The Agency agrees that there are difficulties associated with epidemiologic studies. The relationship between exposure assessments and epidemiologic studies is currently being investigated and will be the subject of a future technical support document and the further refinement of the Guidelines.

V. Clarification of Terminology

A. Exposure vs. Dose

Commentors expressed concern with the American Society for Testing and Materials (ASTM) definition of exposure. Concern was also raised about the assertion that exposures can be estimated when biological tissues for fluid measurements indicate the presence of a chemical. Some commentors found difficulty in the wording of the last sentence in section II.A., specifically "The route of exposure. . .impacts. . .the overall exposure. . . ."

It is the Agency's opinion that the members who served on the ASTM Committee E-47 had expertise in exposure assessment. The scientists and engineers cumulatively possessed many years of experience in exposure assessment. In addition, no technical society has presented an alternate definition of exposure. The Agency will consider changing the definition if a reasonable alternate definition is written and agreed upon by the scientific community.

The Agency agrees with the commentors who were concerned that the wording provided in the Guidelines that the presence of a chemical in biological tissue can be used to estimate exposure is not correct in all cases. Consequently, the word "can" was changed to "may" to reflect the current level of understanding between tissue residue and exposure (II.A., 2nd paragraph, 4th sentence). The Agency agrees with several commentors' concerns that the route of exposure impacts the overall absorbed dose, not the overall exposure, and the Guidelines reflect this change (II.A., last sentence).

B. Mixtures and Synergism

Some commentors thought more discussion was necessary on the effect of chemical mixtures and potential synergistic effect on exposure. The Guidelines for the Health Risk Assessment of Chemical Mixtures includes a discussion of chemical synergism. The Agency recognizes the need to do further work in the area of exposure to mixtures. It is recommended that this be identified as an area requiring further research.

These Guidelines stress the need to determine the products into which the chemical might degrade or react in the environment and to determine if any of these products are ecologically or biologically harmful.

C. Removal and Creation Steps

Some commentors urged that more emphasis be placed on changes that occur once the materials have entered the ambient environment. Other commentors argued that our current understanding will not allow a comprehensive treatment, particularly for metabolic processes.

These Guidelines state the need to address how a chemical agent moves from the source to the exposed population, which may result in the estimation of geographic and temporal distributions in various environmental media. The Guidelines also state the need to know such factors as, for example, whether the chemical agent bioaccumulates or by what mechanism the agent is removed from each medium and the role of any degradation products on ecological safety. We have already stated that guidance for analysis of metabolism data is an area of ongoing research which includes consideration of metabolism data in the calculation of whole organism dose from one species to another.

VI. Purpose, Philosophy, and Results

Several commentors raised questions related to the basic style of the Guidelines. Among the issues raised were:

- the role of exposure assessment in risk assessment/risk management (many comments directed to appropriateness of Figure 1);
- statutory/regulatory authority and uses of results; and
- the need for peer review of assessments and periodic updating of Guidelines.

A deliberate effort to separate risk assessment from risk management has been made. The management of complex issues such as procedural issues, which include coordination or linkage among divisions in the Agency, are best dealt with by management and not in Guidelines.

The decision pathway (Figure 1) was included in the Guidelines at the recommendation of the SAB. It has drawn many comments. The changes suggested would include additional detail and steps that would diminish the value of the graphic. However, the figure has been truncated to remove risk management steps.

In order to remain consistent with the separation of risk assessment and risk management, any directions to consider applicable laws or regulatory decisions have been stricken from the Guidelines.

The Agency agrees that peer review is an important aspect of the assessment process. However, emergency cases may not allow peer review in preliminary assessments. All nonemergency exposure assessments have been peer reviewed and will continue to be peer reviewed. Finally, it is clearly stated in the Guidelines that periodic revision of the document will be done to reflect the benefit of experience and knowledge.

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Exhibit C

Guidance Document

First, Second, and Third Tier Review of Toxic Air Pollution Sources (Chapter 173-460 WAC)

September 2010

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Publication and Contact Information

This document is available on the Department of Ecology's website at www.ecy.wa.gov/biblio/0802025.html.

For more information, contact:

Matt Kadlec
Air Quality Program
P.O. Box 47600
Olympia, WA 98504-7600

(360) 407-6817
matt.kadlec@ecy.wa.gov

Gary Palcisko
Air Quality Program
P.O. Box 47600
Olympia, WA 98504-7600

(360) 407-7338
gary.palcisko@ecy.wa.gov

Washington State Department of Ecology - www.ecy.wa.gov

o	Headquarters, Olympia	360-407-6000
o	Northwest Regional Office, Bellevue	425-649-7000
o	Southwest Regional Office, Olympia	360-407-6300
o	Central Regional Office, Yakima	509-575-2490
o	Eastern Regional Office, Spokane	509-329-3400

Table of Contents

Introduction

Ecology and local air quality agencies use first, second and third tier review to regulate emissions of toxic air pollutants. Hundreds of potentially toxic chemicals are released into the air each year in Washington. Excess exposures to these chemicals can cause serious illnesses and premature deaths. Widespread exposure probably accounts for some of the occurrences of various types of cancers within our population.

This publication is to help toxic air pollution sources understand and use the first, second, and third tier review sections of the notice of construction application. Requirements for first, second, and third tier review are found in Chapter 173-460 Washington Administrative Code (WAC).

First Tier Review

What is first tier review?

First tier review is part of a notice of construction application for a new or modified toxic air pollutant source. It compares your project emissions to the toxic air pollutant values listed in WAC 173-460-150.

How do I know if I need to do a first tier review?

You will need to do a first tier review if potential emissions from your project exceed the de minimis emission levels specified in WAC 173-460-150. Your potential emissions are the expected worst-case emissions from your facility, considering its physical and operational design.

How do I get first tier review?

You do not need to submit a separate petition for first tier review. The notice of construction application you file with the permitting agency serves as your petition for first tier review. Typically, the permitting agency will conduct a first tier review on every notice of construction application it receives.

What issues must I address before the order can be issued?

You must show that the emission increases from all new or modified emission units are below the acceptable source impact level (ASIL):

- after application of best available control technology for air toxics (tBACT); and
- at any location outside of your property boundary.

You can find the ASILs in WAC 173-460-150.

How can I show that emissions are below the ASIL?

You can show emissions are below the ASIL by:

- demonstrating that the emissions are at or below the small quantity emission rates (SQER);
- using a screening model (such as AERSCREEN); or
- using a refined air dispersion model (such as AERMOD).

What can I do if emissions exceed the ASIL?

You have several options, including:

- revise the project and application;
- negotiate an enforceable limit;
- off-set the emissions by reducing emissions from another on-site emission unit;
- submit a second tier petition;
- submit a third tier petition; or
- withdraw the application.

How do I off-set the new emissions by reducing them at another emission unit?

You must meet several criteria in order to get this option approved:

- the emission reductions must be actual reductions;
- the reductions must be modeled against all affected receptors; and
- when the emission increases and reductions are modeled together at the receptor, the modeling must demonstrate that the off-set proposal results in emission values lower than the ASIL.

Who approves a first tier analysis?

Your permitting agency will review the first tier analysis and either approve or deny it.

What happens if my first tier analysis is approved?

If your permitting agency approves the first tier analysis, it will include the approval decision in an "Order of Approval." For permits issued by Ecology, guidelines for issuing this order and requirements for notifying the public are in WAC 173-400-110. Other permitting agencies may have their own guidelines. The order may contain the following:

- emission limits for each toxic air pollutant (TAP) subject to review;
- a method of assuring compliance with TAP limits (usually monitoring, reporting, and operation restrictions);
- a statement of the Best Available Control Technology for Air Toxics (tBACT) for each TAP; and
- enforcement criteria for voluntary emission reductions, including monitoring, record-keeping, and reporting requirements.

What happens if my first tier analysis is not approved?

If emission increases still exceed the ASIL and other options do not work, you can submit a petition for second tier review.

Are there any exemptions from the first tier review process?

Yes. A list of exemptions from new source review is in WAC 173-400-110. Also, your permitting agency might have its own list of exemptions. Exemptions for toxic air pollutants and criteria pollutants are related because the permit process procedures, definitions, and exemptions are the same for both.

Exemptions are divided into two broad categories:

- emission unit and activity exemptions; and
- exemptions based on emissions.

To see if your project is exempt, read the emission unit and activity listing in WAC 173-400-110(4 and 5), and contact your permitting agency. De minimis emission values for toxic air pollutants are in WAC 173-460-150. You must consider all of the new or modified emission units together. For the project to be exempt, emissions from all of the individual emission units added together must be below the de minimis values.

Second Tier Review

What is second tier review?

Like first tier review, second tier review is part of a notice of construction application for a new or modified toxic air pollutant source. You need to do a second tier review if any of your project's toxic air pollutant emissions exceed the ASIL after you have completed a first tier review. In this step of the notice of construction application process, the applicant submits a health impacts assessment to Ecology. Ecology will review the health risks associated with your project.

How do I get second tier review?

Submit a petition for second tier review to Ecology, with a copy to the permitting agency that has jurisdiction. The application form includes the Health Impact Assessment Checklist and is available at: http://www.ecy.wa.gov/biblio/ecy070415.html

What is the review process for a second tier petition?

Ecology's air toxics engineer, toxicologist, and air quality modeler work together on second tier petitions. The review process includes:

- pre-application conference;
- a second tier petition and payment of applicable fees;
- HIA protocol; and
- HIA document.

Pre-application conference

After Ecology is notified that a proposed project requires second tier review, Ecology recommends you have a pre-application conference with Ecology staff before you submit a second tier petition. The pre-application conference:

- helps you identify regulatory issues before you commit a significant amount of time and resources toward a specific course of action;
- lets you know early in the process what you need to address in the Health Impact Assessment, which can avoid unnecessary delays later on; and
- helps you identify the review criteria for your project, so that you can present your proposal accurately.

You and your consulting team need to attend the conference. The team typically includes an engineer, plant operations manager, and other specialists involved in your proposal. You and your team will meet with an Air Quality Program engineer, toxicologist, and air quality modeler.

The permit writer who reviewed your first tier analysis will also attend, whether they work for Ecology or a local air quality agency.

At the conference, you, your team, and Ecology staff will review the following information:

- required permits, approvals, and fees;
- protocol for the health impact analysis;
- the refined air dispersion modeling methods used to estimate TAP levels;
- typical project review timelines;
- application regulations;
- the public hearing process; and
- any other questions you might have.

The amount of information Ecology can give you at the conference depends on the level of detail you provide about the project. Because the conference takes place early in the process, Ecology will not be able to anticipate all the relevant project details. Ecology will give you a protocol to follow that tells you what to do next.

The conference **will not** provide:

- a detailed toxicology analysis or modeling review; or
- a final recommendation on a proposal.

To schedule a pre-application conference, call Matt Kadlec at (360) 407-6817 or Gary Palcisko at (360) 407-7338. They will work with you to find a time that works for everyone. The conference is typically held at Ecology's Headquarters building at:

300 Desmond Drive SE
Lacey, WA 98503

Second tier review petition and fees

After the pre-application conference, the applicant submits to Ecology a petition and applicable fees for second tier review, with a copy to the permitting agency that has jurisdiction. The application form includes the Health Impact Assessment Checklist and is available at: http://www.ecy.wa.gov/biblio/ecy070415.html. You can find more information on applicable fees starting on page 31.

HIA protocol

The applicant must also submit an HIA protocol. Ecology will review the HIA protocol after the applicant submits the $10,000 initial fee with the HIA protocol and completed second tier application. Basic information required for HIA protocol is included later in this document.

HIA document

After Ecology approves the HIA Protocol, the applicant prepares and submits an HIA document. Ecology toxicologists will review the HIA to determine if health impacts are adequately characterized. Ecology will provide substantive and non-substantive comments on the HIA document and will request the applicant revise the HIA document if necessary. This process can be repeated until the applicant prepares an acceptable final HIA document. Ecology's project engineer or delegate will review portions of the HIA that involve the project's engineering specifications. Likewise, Ecology's dispersion modeler will review portions of the HIA that involve toxic air pollutant (TAP) concentration modeling. Following confirmations by the engineer and modeler, Ecology's project toxicologist will review risk assessment portions of the HIA. The toxicologist will then communicate to all parties the results of the HIA review.

Once an acceptable HIA document has been prepared, Ecology will prepare a brief staff report which summarizes Ecology's review of the HIA and includes recommendation(s) to the local permitting authority about the petition. Ecology will:

- post the applicant's final HIA document, Ecology's staff report, and Ecology's cover letter on Ecology's air toxics review web page (http://www.ecy.wa.gov/programs/air/Tier2/Tier2_infosite.html);
- make a final recommendation for approval or denial of the project; and
- send the recommendation to you and the permitting agency, which issues the actual approval order.

Ecology's decision on the second tier petition must be included in the final decision on the notice of construction application.

Who approves a petition for second tier review?

Only Ecology staff can review, approve, or deny a second tier petition.

What materials should I provide, and when?

In the pre-application conference, you will be given a protocol for preparing the required documentation for the second tier petition. After the pre-application conference, the permitting agency (either a local air quality agency or one of Ecology's regional offices) will provide a preliminary order of approval directly to Ecology. Then, follow this protocol to provide information:

Provide to Ecology:

- the results of the refined air dispersion modeling for all pollutants that exceed the SQERs; and
- a full copy of the second tier petition (containing a Health Impacts Assessment).

Provide to the permitting agency that reviewed your first tier analysis:

- a full copy of the second tier petition.

Is public involvement required?

Yes. Public involvement is required for any project that needs a second tier review. It may be limited to a public notice and public comment period, or Ecology may determine that a public hearing is needed. If a public hearing is held, Ecology and the permitting agency will hold a joint public hearing to streamline the public review process. Ecology staff will explain the second tier recommendation at the public hearing. You and your consultants should be prepared to explain your project and answer questions at the public hearing.

What can I do if Ecology does not approve the second tier petition?

If Ecology denies the second tier petition, the permitting agency may not approve the project. At that point, you have the following options:

- revise the project and application;
- propose emission reductions from an off-site emission unit;
- submit a third tier petition; or
- withdraw the application.

My project triggers second tier review. Are there any exemptions from the second tier review process?

No. If your project triggers second tier review, you must submit a second tier petition to Ecology before your project can be approved. If you think that your project will not meet the approval criteria of a second tier review, you may opt to submit a third tier petition instead of a second tier petition.

Third Tier Review

What is third tier review?

You can submit a petition for third tier review if the health risks from your project exceed the second tier review thresholds. In third tier review, your petition requests that the director of Ecology approve the project based on a risk management analysis.

How do I submit a petition for third tier review?

Submit your petition for third tier review to Ecology, with a copy to the permitting agency that has jurisdiction.

What materials should I provide, and when?

The materials required for a third tier review are the same as for a second tier review. You may submit the third tier petition at the same time you submit the second tier petition. Prior denial of a second tier petition submitted under WAC 173-460-090 is not required. The permitting agency (either a local air quality agency or one of Ecology's regional offices) will provide a preliminary order of approval directly to Ecology. Then follow this protocol to provide information:

Provide to Ecology:

- the results of the refined air dispersion modeling for all pollutants that exceed the SQERs;
- a full copy of the third tier petition (containing a health impacts assessment); and
- a description of environmental benefits of the proposal.

Provide to the permitting authority that reviewed your first tier analysis:

- a full copy of the third tier petition.

In addition to the above documentation, you may propose voluntary measures to reduce community exposure to pollutants emitted by your project. Voluntary measures might include voluntary reduction of emissions from existing unmodified emissions units at your facility or at another facility.

What is the review process for a third tier petition?

Ecology's air toxics engineer, toxicologist, and air quality modeler work together to prepare a recommendation to the director of Ecology to either approve or deny a third tier petition. Within 30 days after you've submitted the petition, Ecology will:

- review it for completeness; and
- provide you a letter stating the petition is complete or listing needed information if it is not complete.

Within 60 days after determining that your petition is complete, Ecology will:

- write a draft technical support document and send it to you and the permitting agency for review and comment;
- address any questions or concerns brought up during review;
- together with you, initiate a minimum 30-day public notice and public comment period;
- together with you, schedule a public hearing.

After the public hearing, Ecology will review and address all comments. Ecology will then prepare the final recommendation and technical support document, and send them to you and the permitting authority, which issues the actual approval order.

Ecology's final recommendation on the third tier petition must be included in the final decision on the notice of construction application.

What criteria will Ecology follow to approve or deny a petition for third tier review?

Before approving your third petition, Ecology's director must find that the following conditions are met:

- proposed emission controls represent at least tBACT;
- a health impact assessment addressing all of Ecology's requirements has been completed; and
- approval of the project will result in a greater environmental benefit to the state of Washington.

Is public involvement required?

Yes. Public involvement is required for any project that needs a third tier review. The public involvement process must include a public notice and public comment period, as well as a public hearing. The purpose of the public hearing is to present the results of the third tier review and to

answer any questions from the public. You and your consultants should be prepared to explain your project and answer questions at the public hearing.

What can I do if Ecology does not approve the third tier petition?

If Ecology denies the third tier petition, the permitting agency may not approve the project. At that point, you have the following options:

- revise the project and application;
- propose emission reductions from an off-site emission unit; or
- withdraw the application.

My project triggers third tier review. Are there any exemptions from the third tier review process?

No. If your project triggers third tier review, you must submit a third tier petition before your project can be approved.

Health Impact Assessment

This section helps toxic air pollution sources prepare a health impact assessment (HIA) as part of second tier or third tier review, as required in Chapter 173-460 WAC. Ecology's Air Quality Program recommends that permit applicants preparing an HIA refer to the Air Toxics Hot Spots Program Guidance Manual for Preparation of Health Risk Assessments, published in March 2015 by the Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. (See the citation list at the end of this document.)

The guidance manual addresses the techniques used to assess health risks of airborne contaminants released by new or modified stationary sources like those permitted in Washington. Most of the techniques described in the Hot Spots Program Guidance Manual are common to other regulatory risk assessment applications. However, applicants may need additional analyses depending on their unique circumstances. Applicants should contact Ecology before beginning work on their HIA in order to assure that all WAC 173-460-090 requirements will be satisfied. In general, using the Hot Spots Program Guidance Manual risk assessment procedures and report presentation will speed up Ecology's review. It will also minimize the chance that applicants will need to revise and resubmit their HIA.

What is an HIA?

An HIA looks at how emissions of toxic air pollutants from a specific project will affect public health. It involves several steps, including hazard identification, exposure analysis, toxic response, and risk characterization.

Who needs to submit an HIA?

Second and third tier petitions always need an HIA.

How do I submit an HIA?

When you submit a petition for a second or third tier review, the HIA will be included in your pre-application conference.

Why do I need a pre-application conference?

Pre-application conferences help you learn about regulatory issues before you commit a significant amount of time and resources to a specific course of action. At the pre-application conference, Ecology will tell you what issues need to be addressed in the HIA. This will help you avoid unnecessary costs and delays.

What documentation do I submit with an HIA?

Because each HIA is tailored to fit a specific project, each one may require different documentation. Generally, you will need to include:

- A map of the site and neighborhood showing:
    - location of new or modified emission points;
    - local zoning of the affected area;
    - locations of and distances (in meters) between the sources; and
    - residences, businesses, roadways, public properties, and public or private facilities serving population subgroups such as schools, nursing homes, hospitals, and for certain TAPs, private and public drinking water wells (note the well depth).

- Hazard identification, including:
    - a list of all TAPs (as defined in Chapter 173-460 WAC) that will be emitted by the facility, and
    - a physical description of those TAPs.

For details, refer to the sections below titled "Dispersion Modeling Protocol and Report Contents," "Contents of the Health Impact Assessment," and "Outline of the Health Impact Assessment Report."

What do I need to submit about the TAP concentrations?

You must show how you derived the TAP concentration levels. Include the following:

- emission rates, in grams per unit of time, at the maximum possible rate;
- modeled concentration estimates in $\mu g/m^3$ or ppb (disclose the emissions factors used in modeling);
- any available monitoring measurement results; and
- any uncertainties and assumptions in deriving concentration levels.

You must also disclose the cross-media transport of the emissions in the environment, the environmental persistence, the degradation pathways, and the final fate of the toxic air pollutants. This means describe the movement of proposed toxic air emissions from air into water and/or soil which people may be exposed to. Generally, the inhalation pathway of exposure is the largest contributor to the total dose. However, there are situations where a non-inhalation pathway contributes substantially to total dose. You can get detailed guidance on this subject from a variety of authorities, for example EPA's Guidelines for Exposure Assessment (1992) and Exposure Factors Handbook (2011) and OEHHA's Air Toxics Hot Spots Program Guidance Manual for Preparation of Health Risk Assessments (2015, chapter five). (See the citation list at the end of this document.)

What materials must I include to assess exposure?

You must identify the TAP exposure pathways, including the following:

- Disclose the total daily intake of TAPs attributable to the project source as well as the background sources. EPA has some ambient air concentration estimates in their NATA database.
- Estimate the durations of exposure, including long-term averages, short-term peaks and worst-case scenarios. Detail the exposure parameters associated with sensitive population subgroups. You can get detailed guidance on this subject from a variety of authorities, including EPA's Guidelines for Exposure Assessment (1992) and Exposure Factors Handbook (2011) and OEHHA's Air Toxics Hot Spots Program Guidance Manual for Preparation of Health Risk Assessments, (2015, chapter five). (See the citation list at the end of this document.) Identify the potentially exposed populations. Give special emphasis to any subpopulations that might be unusually susceptible to any TAPs emitted by your project.
- Using the information on the location of potentially exposed populations, show the TAP concentrations at the points where people might be exposed to the pollutants in question.

What issues do I need to address in the toxicity discussion?

The toxicity discussion should focus on the effects relevant to the proposed toxic air pollutant concentrations. The following issues should be thoroughly discussed:

- toxic effects of the toxic air pollutants;
- exposure levels associated with specific effects;
- exposure patterns and duration of exposure as established by studies of the toxic effects;
- any quantitative, chronic toxicity values including:
    - inhalation reference concentration or similar hazard-based concentrations;
    - cancer unit risk factor estimates;
    - slope factor or carcinogenic potency estimates; and
- any quantitative intermediate and short-term acute toxicity values.

What issues do I need to address in the risk/hazard assessment section?

Provide a discussion of offsetting reductions in risk that might accrue to society as a result of completing the proposed facility modification. This typically includes a:

- qualitative discussion of the risks;
- quantitative discussion of the risks with appropriate toxicity measures, calculated cancer risks, and the hazard index;
- discussion of uncertainties in the risk assessment;

- discussion of acceptability of risk with regard to guidelines in Chapter 173-460 WAC; and
- discussion of the extent to which the proposed facility might affect human health.

What issues do I need to address in the uncertainty section?

There is always some level of uncertainty associated with risk assessment. While uncertainty encompasses those factors that are not known, and could be eliminated or reduced with scientific studies, we are not asking you to conduct original research. We want you to disclose your level of confidence in the data used to substantiate your conclusions.

Risk can be over or underestimated because of many factors, including:

- extrapolation of toxicity data in animals to humans;
- uncertainty in the estimation of emissions;
- uncertainty in the air dispersion models;
- interactive effects of exposure to more than one carcinogen or toxicant;
- uncertainty in the exposure estimates; and
- uncertainty about the extent of toxicant susceptibility variation within human populations.

The HIA mentions subpopulations. What is an example of a sensitive or understudied subpopulation?

Children are a subpopulation whose hematological nervous, endocrine, and immune systems are still developing. They may be more sensitive to the effects of carcinogens on their developing systems. These sensitivities are not included in the worker population and risk estimates based on occupational epidemiological data, which are based on adult populations.

Who reviews the HIA?

Ecology's Air Quality Program toxicologists review HIAs. While the toxicologists are reviewing the HIA, the engineer and dispersion modeling staff review other portions of the second or third tier petition. They determine if tBACT and refined modeling are sufficient.

Note that though Ecology's toxicologists review HIA documentation; they are not authorized to prepare the applicant's assessment.

What can I do if Ecology does not approve the HIA?

You have the following options:

- revise the project and application;
- propose emission reductions from an off-site or on-site emission unit;
- submit a third tier petition (See WAC 173-460-100); or
- withdraw the application.

Where can I get more information on the HIA?

Contact either of the Air Quality Program toxicologists:

Matt Kadlec
(360) 407-6817
matt.kadlec@ecy.wa.gov

Gary Palcisko
(360) 407-7338
gary.palcisko@ecy.wa.gov

Contents of the Health Impact Assessment Protocol

Applicants must submit a Health Impacts Assessment Protocol before submitting a draft HIA. The protocol ensures that the applicant will submit sufficient information and is intended to prevent delays caused by incomplete analyses. The protocol should contain a description of how the applicant intends to estimate the health impacts posed by TAPs subject to second tier review. Generally, an applicant will need to provide an air quality analysis that demonstrates compliance with both national ambient air quality standards and toxics review. The following items need to be included in the Health Impact Assessment Protocol:

Emissions Estimate

- Quantify short- and long-term emission rates,
  - mass per hour, day, year;
- Report emission factors and their source and justification;
- Report applicable emission standards and ASILs;
- Provide background concentrations, if known.

Source Characteristics

- Site plan showing fence line, emission units, and other structures;
- Modeling parameters.

Model and Model Assumptions

- AERMOD is to be used in most situations.

Meteorology

- Identify representative surface meteorological data.
  - 5 years of continuous quality-assured/quality-controlled meteorological data/QC'd upper air data

Receptor Grid

- Recommended receptor grid spacing to ensure that sampling error does not reduce the maximum computed concentration by more than 10%:

Distance from Source [m]	Grid Spacing [m]
0 – 150	12.5
150 – 400	25
400 – 900	50
900 - 2000	100
2000 - 4500	300
> 4500	600

Deposition

- For some TAPs, applicants may need to estimate deposition so that multi-pathway exposures can be assessed. These TAPs include:

    - 4,4'-Methylene dianiline
    - Creosotes
    - Diethylhexylphthalate
    - Hexachlorocyclohexanes
    - PAHs
    - PCBs
    - Cadmium & compounds
    - Chromium VI and compounds
    - Inorganic arsenic and compounds
    - Beryllium and compounds
    - Lead and compounds
    - Mercury and compounds
    - Nickel
    - Fluorides (including hydrogen fluoride)
    - Dioxins and furans

Model Output/Results

- Files provided to Ecology
- Modeling results to be used to demonstrate compliance or assess risk

Receptors

- Identify receptors where the ASIL is exceeded.
  - Identify maximally-exposed residential, workplace receptors and point(s) of maximum impact. (**Note**: Maximally-impacted receptors around a site can vary depending on concentration averaging time.)

Short-term and long-term risk-based exposure concentrations

Depending on which chemicals are being evaluated and the type of receptor that is impacted, short-term and/or long-term ambient concentrations are needed.

- Short-term = typically 1-hr., 8-hr., 24-hr. concentrations
- Long-term = typically annual average concentration

Acute and chronic non-cancer hazard (1-hr., 8-hr., 24-hr., annual exposure concentrations)

For all non-carcinogenic toxic air pollutants exceeding their SQERs:

- Identify relevant short-term and long-term non-cancer toxicity values for chemicals exceeding SQERs
  - For example: EPA RfCs, OEHHA RELs, ATSDR MRL

- Calculate Hazard Quotients (HQ)
  - Exposure concentration ($\mu g/m^3$) divided by risk-based concentration ($\mu g/m^3$)

- For multiple chemicals with similar toxic effects (i.e., same tissue or organ system), calculate Hazard Index
  - Sum hazard quotients with same averaging time and similar toxic effects for all toxic air pollutants that exceed the SQER

- Determine the frequency and geographic extent that short- and long-term concentrations exceed relevant toxicity values (i.e., HQs > 1)

Cancer risk (annual exposure concentrations)

For all carcinogenic toxic air pollutants exceeding their ASILs and SQERs:

- Identify existing inhalation unit risk factors or cancer potency factors
- Calculate lifetime increased cancer risk from exposure to each TAP
- Calculate the sum of cancer risks for all chemicals emitted in excess of SQER to produce the total increased cancer risk from project
- Identify population exposed in excess of one per million and estimate total population risk from project

Outline of the Health Impact Assessment Report

In general, the HIA should provide information about:

- Project description
- Emissions
- Air dispersion modeling
- ASIL screening
- Risk assessment
  - Hazard identification, exposure, dose-response (which criteria are used to estimate risk), risk characterization, uncertainty
  - Discussion of acceptability of risk

Recommended Outline of an HIA

Note: Not every item below will be required in every HIA report. Ecology staff will discuss the specific requirements of your HIA report during the pre-application meeting.

Project description

- Project overview
- Physical location
  - Address, city, county
  - Land use (zoning) in areas adjacent to project
  - Site map showing emission points, property boundary, off-site receptors (outside any limited public access boundary maintained around the facility, and the locations of any buildings and their usage (i.e., housing, business, school, etc.))

SQER and ASIL comparison

- Comparison of facility emission rates of TAPs to their respective SQER
  - Model concentrations of those that exceed their SQER
  - Compare results to their ASIL(s)
- Refined dispersion modeling to estimate off-site concentration of those TAPs to their respective ASILs
- If a chemical exceeds its ASIL at an off-site location, then a health impact assessment is performed.

Hazard identification

- Identification of the TAPs that may pose a threat to human health (those that exceed ASILs and those that exceed SQERs with similar effects).
- Physical description of the TAP (s) emitted in amounts greater than their SQER and overview of each chemical's toxicity (i.e., affected tissue/organ and the critical effect. For example, acrolein: Eyes and respiratory tract; eye irritation and respiratory epithelium lesions).
- Potential for cross-media transport in the environment, environmental persistence, degradation pathways, and final fate of the TAP(s). Provide public water solubility data, and degradation half-lives in air, water, and soil.

Identification of places with potentially-exposed people (off-site)

- For example, residences, businesses, parks, schools, hospitals within the geographic extent where estimated concentrations are greater than the ASIL.

Discussion of TAP concentrations

- Using the information on location of potentially-exposed populations, TAP concentrations that exceed ASIL(s) should be given at points where humans might come into contact with the TAP(s).
- Derivation of the concentration levels should be discussed.
- Concentration estimates, in $\mu g/m^3$ by modeling and emissions factors used in modeling.
  - Averaging times may vary depending on the project and potentially-exposed receptors, but examples are:
    - Maximum 1-hr., 8-hr., and 24-hr. exposure – for chemicals that have the potential to cause acute effects over a short time
    - Annual average exposure – for chemicals that have the potential to cause cancer or other chronic effects
    - Display results on maps

Exposure assessment

- Identification of TAP exposure pathways
- Development of total daily intake attributable to source and background sources (existing ambient air concentration estimates for some pollutants are available in EPA's NATA)
  - Durations of exposure, including long-term averages, short-term peaks, and worst-case scenarios
  - Exposures at maximally-effected residence(s), business(es), and fence line (limited public access boundary) places
  - Exposure parameters associated with sensitive population subgroups. For example, situations where children may be frequently exposed may warrant child-specific exposure parameters.

Toxicity (should focus on effects relevant to proposed TAP concentrations)

- Description of toxic effect(s)
- Exposure levels associated with effect(s)
- Exposure pattern and duration of exposure in studies of toxic effects
- Any quantitative, chronic toxicity values
  - Inhalation reference concentration or similar hazard-based concentrations
  - Cancer unit risk factor estimates
  - Oral risk based concentrations for substances evaluated through multi-pathways of exposure
- Quantitative intermediate/short-term toxicity values
- Discussion of how the site-specific toxicity value considers exposure duration and frequency at the site

Risk/hazard characterization

- Qualitative discussion of the risk(s)
- Quantitative discussion of the risk(s)
  - With appropriate measure(s) of toxicity
  - Calculated cancer risk(s)
- Hazard quotients and hazard indexes, if there are any co-acting combinations of TAPs. (Critical effect –specific hazard indexes for TAPs emitted at rates above their SQERs for any co-acting combination of such TAPs.)

Discussion of uncertainty and variability of numeric values used in the HIA

A HIA is composed of many numeric values – each with its own uncertainty and/or variability. Uncertainty is that which is not known about a factor that influences its value. Variability occurs when a quantity that is repeatedly measured exhibits values that differ. It can be quantified using descriptive statistics such as the range.

Discussion of acceptability of risk with regard to guidelines in Chapter 173-460 WAC

- Increased cancer risk is no more than 10 per million
- Non-cancer hazard quotients or indexes are less than one, or Ecology determined that non-cancer hazards are acceptable

Second and Third Tier Review Timeline

Step 1: Applicant submits to Ecology:

- full copy of the second or third tier petition (including all of the elements discussed in the HIA protocol);
- results of the refined air dispersion modeling for all pollutants that exceed the ASILs;
- preliminary order of approval issued by the permitting agency (The permitting agency will generally provide the preliminary order of approval directly to Ecology. The permitting agency is either a local air quality agency or one of Ecology's regional offices.); and
- description of environmental benefits of the proposal (for a **third tier petition**).

Step 2: Within 30 days after receiving the petition, Ecology will:

- review it for completeness; and
- issue a letter stating the petition is complete or list all information needed to complete the petition.

Step 3: Within 60 days after determining a petition is complete, Ecology will:

- write a draft technical support document and send it to the applicant and permitting agency for review and comment;
- address any questions or concerns brought up during that review;
- for a **second tier petition**, make a final decision to recommend approval or denial of the project, and send the **final second tier** recommendation to the applicant and the permitting agency;
- for a **third tier petition**, prepare a third tier review recommendation and technical support document for public comment, and send them to the applicant and the permitting agency.

Step 4: Permitting agency initiates a public comment period on the draft notice of construction approval

After receiving Ecology's recommendation on the second or third tier petition, the permitting agency and the applicant must:

- provide a minimum 30-day public notice and a public comment period before approving or denying a notice of construction application involving second or third tier review;
- include the draft notice of construction approval order and Ecology's recommendation on the second or third tier petition as part of the public review documents;

- hold a public hearing to discuss the third tier petition and to answer questions from the public; and
- in consultation with Ecology, address any questions or concerns brought up during the public comment period.

Step 5: Final approval or denial of the project by the permitting agency

- If Ecology recommends approval of the project, the permitting agency may approve the notice of construction application.
- If Ecology recommends denial of the project, the permitting agency may not approve the project.

Second and Third Tier Review Fees

Purpose

This section explains second and third tier review fees and key process changes to applicants and consultants who submit health impact assessments under Chapter 173-460 WAC. These changes were prompted by a 2011 fee rule that changes the way Ecology collects fees and charges time for work spent reviewing health impact assessment documents.

Background

Beginning July 1, 2011, Ecology changed the fee schedule for permitting activities covered under our new source review program. These fee increases, which were authorized by the 2011 legislature, must support the cost of issuing a permit. Ecology accomplishes this by collecting an initial fee with the application that will cover a set number of review hours (base hours), depending on application type and a $95 per hour fee for the hours above base needed to complete the review and issue the permit. A notice summarizing all of the changes made by Ecology to the permitting fees regulation is available at http://www.ecy.wa.gov/biblio/1102028.html.

How the 2011 Fee Structure Affects Second and Third Tier Review

Under the 2011 fee structure, each member of Ecology's toxics review team will provide approximately 2 hours of pre-application assistance to the applicant. Time spent on pre-application assistance will not be counted toward the permit fee (not toward the initial fee or any additional fee) billed to the applicant, and will be provided in the form of one meeting between the applicant and Ecology, as well as any required advanced preparation for that meeting. Our goal in this pre-application assistance is to provide you with the majority of the information you need to prepare your health impact assessment protocol for submission to Ecology.

Once Ecology has provided information in the meeting, we will still be available to offer limited guidance to you as you prepare your protocol; however, the next step is for you to submit a health impact assessment (HIA) protocol along with the initial review fee of $10,000. The fee must be submitted with the protocol to Ecology's fiscal office before Ecology will review or approve the HIA protocol.

The HIA protocol must be accompanied by a completed application for second or third tier review. The application form includes the Health Impact Assessment Checklist and is available at http://www.ecy.wa.gov/biblio/ecy070415.html.

Alternate Method for Continuing Discussions with Ecology

It is our goal that you know how to proceed to develop the HIA by the end of the pre-application meeting. If you think your project needs more than a 2-hour meeting with Ecology, you have three choices:

- Submit the Application for Second Tier Review or Third Tier Review along with your $10,000 check. Ecology will meet with you to help you prepare your HIA and we will track our time against your initial fee.
- Enter into a contract with Ecology for additional upfront work. The rate is $95 per hour. We charge the same rate for working on your project under either option.
- Request Ecology stop working on the project once the 2 hours of "free" (included in the initial review fee) pre-application assistance are used up.

The Initial Fee You Submit May Not Cover the Cost of Processing Your Petition

The $10,000 initial fee you submit covers up to 106 hours of Ecology's review time. Ecology will track the number of hours spent on your project and will notify you when we approach the 106 hours covered by the initial fee. If the total number of review hours exceeds 106 hours, Ecology will bill you $95 per hour for each additional hour worked. We will bill you at the end of the process just before we issue a final decision. You must pay the bill before Ecology will issue a decision on your petition.

Public Hearing

The applicant is responsible for costs associated with a public hearing, if one is held. This includes staff time to prepare for the public hearing, travel time to and from the public hearing, time spent conducting the public hearing, time spent responding to public comments, and publications costs for a newspaper notice.

Changes to HIA Review Procedure

Ecology's goal is to complete our review of the HIA in a timely manner so that applicants are not charged additional hourly charges. To accomplish this goal, Ecology has changed the way we review the health impact assessment. The primary changes to our review procedure include:

- Ecology will provide the minimum amount of pre-application assistance necessary to advise the applicant of the demonstrations and submittals necessary to meet permitting requirements (one meeting lasting about 2 hours).

- Ecology will review the HIA protocol after the applicant submits the $10,000 initial fee with the HIA protocol and complete second or third tier application. The HIA protocol review process can be one of continuous improvement, until an acceptable HIA protocol has been prepared.

- Based on the approved HIA protocol, the applicant will prepare and submit an HIA document for review by Ecology.
- Ecology will provide substantive and non-substantive comments on the HIA document and will request the applicant revise the HIA document, as necessary. This process can be one of continuous improvement, until an acceptable final HIA document has been prepared by the applicant. Ecology's project engineer or delegate will review portions of the HIA that involve the project's engineering specifications. Likewise, Ecology's meteorological modeler will review portions of the HIA that involve toxic air pollutant (TAP) concentration modeling. Following confirmations by the engineer and modeler, Ecology's project toxicologist will review risk assessment portions of the HIA. The toxicologist will then communicate to all parties the results of their review of the HIA.
- Once an acceptable HIA document has been prepared, Ecology will prepare a brief staff report which summarizes Ecology's review of the HIA and includes a recommendation(s) to the local permitting authority regarding the petition.
- Ecology will post the applicant's final HIA document and Ecology's staff report and cover letter on Ecology's air toxics review web page.

Who to Contact for More Information

For more information, contact:

Gary Palcisko
Washington State Department of Ecology
Air Quality Program
P.O. Box 47600
Olympia, WA 98504-7600
(360) 407-7338
gary.palcisko@ecy.wa.gov

Matt Kadlec, PhD, DABT
Washington State Department of Ecology
Air Quality Program
P.O. Box 47600
Olympia, WA 98504-7600
(360) 407-6817
matthew.kadlec@ecy.wa.gov

Citations

Air Toxics Hot Spots Program Guidance Manual for Preparation of Health Risk Assessments, Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Oakland, CA, March 2015 (http://oehha.ca.gov/air/hot_spots/hotspots2015.html)

U.S. EPA. Guidelines for Exposure Assessment. U.S. Environmental Protection Agency, Risk Assessment Forum, Washington, DC, EPA/600/Z-92/001, 1992. (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=15263)

U.S. EPA. Exposure Factors Handbook 2011 Edition (Final). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-09/052F, 2011. (http://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252)

Exhibit D

EPA/630/R-03/003F
March 2005

Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens

Risk Assessment Forum
U.S. Environmental Protection Agency
Washington, DC 20460

DISCLAIMER

This document has been reviewed in accordance with U.S. Environmental Protection Agency policy and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

AUTHORS AND CONTRIBUTORS

This document was prepared by a Technical Panel of the Risk Assessment Forum.

AUTHORS

Hugh Barton, National Health and Environmental Effects Research Laboratory, ORD
Jim Cogliano, National Center for Environmental Assessment, ORD
Michael P. Firestone, Office of Children's Health Protection, OA
Lynn Flowers, National Center for Environmental Assessment, ORD
R. Woodrow Setzer, National Health and Environmental Effects Research Laboratory, ORD
Larry Valcovic, National Center for Environmental Assessment, ORD
Tracey Woodruff, Office of Policy, Economics, and Innovation, OA

CONTRIBUTORS

Neepa Choksi, Fellow to the Office of Solid Waste and Emergency Response
Resha M. Putzrath, Risk Assessment Forum Staff, National Center for Environmental Assessment, ORD
William P. Wood, Risk Assessment Forum Staff, National Center for Environmental, ORD

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CONTENTS

LIST OF FIGURES

PREFACE

U.S. Environmental Protection Agency (EPA or the Agency) cancer risk assessments may be conducted differently than envisioned in this Supplemental Guidance for many reasons including, for example, new information, new scientific understanding, or different science policy judgment. The practice of risk assessment with respect to accounting for early-life exposures to toxicants continues to develop, and specific components of this Supplemental Guidance may become outdated or may otherwise require modification in individual settings. It is EPA's intent to use, to the extent practicable and consistent with Agency statutes and regulations, the best available science in its risk assessments and regulatory actions, and this Supplemental Guidance is not intended to provide any substantive or procedural obstacle in achieving that goal. Therefore, the Supplemental Guidance has no binding effect on EPA or on any regulated entity. Where EPA does use the approaches in the Supplemental Guidance in developing risk assessments, it will be because EPA has decided in the context of that risk assessment that the approaches from the Supplemental Guidance are suitable and appropriate. This judgment will be tested through peer review, and the risk assessment will be modified to use different approaches if appropriate.

This Supplemental Guidance is intended for guidance only. It does not establish any substantive "rules" under the Administrative Procedure Act or any other law and has no binding effect on EPA or any regulated entity, but instead represents a non-binding statement of policy.

The Supplemental Guidance addresses a number of issues pertaining to cancer risks associated with early-life exposures generally, but provides specific guidance on potency adjustment only for carcinogens acting through a mutagenic mode of action. This guidance recommends for such chemicals, a default approach using estimates from chronic studies (i.e., cancer slope factors) with appropriate modifications to address the potential for differential risk of early-lifestage exposure. Default adjustment factors are meant to be used only when no chemical-specific data are available to assess directly cancer susceptibility from early-life exposure to a carcinogen acting through a mutagenic mode of action.

The Agency considered both the advantages and disadvantages of extending the recommended, age dependent adjustment factors for carcinogenic potency to carcinogenic agents for which the mode of action remains unknown. EPA recommends these factors only for carcinogens acting through a mutagenic mode of action based on a combination of analysis of available data and long-standing science policy positions that set out the Agency's overall approach to carcinogen risk assessment, e.g., the use of a linear, no threshold extrapolation procedure in the absence of data in order to be health protective. In general, the Agency prefers

to rely on analyses of data rather than on general defaults. When data are available for a susceptible lifestage, they should be used directly to evaluate risks for that chemical and that lifestage on a case-by-case basis. In the case of nonmutagenic carcinogens, when the mode of action is unknown, the data were judged by EPA to be too limited and the modes of action too diverse to use this as a category for which a general default adjustment factor approach can be applied. In this situation per the Agency's *Guidelines for Carcinogen Risk Assessment*, a linear low-dose extrapolation methodology is recommended. It is the Agency's long-standing science policy position that use of the linear low-dose extrapolation approach (without further adjustment) provides adequate public health conservatism in the absence of chemical-specific data indicating differential early-life susceptibility or when the mode of action is not mutagenicity.

The Agency expects to produce additional supplemental guidance for other modes of action, as data from new research and toxicity testing indicate it is warranted. EPA intends to focus its research, and to work collaboratively with its federal partners, to improve understanding of the implications of early life exposure to carcinogens. Development of guidance for estrogenic agents and chemicals acting through other processes resulting in endocrine disruption and subsequent carcinogenesis, for example, might be a reasonable priority in light of the human experience with diethylstilbesterol and the existing early-life animal studies. It is worth noting that each mode of action for endocrine disruption will probably require separate analysis.

As the Agency examines additional carcinogenic agents, the age groupings may differ from those recommended for assessing cancer risks from early-life exposure to chemicals with a mutagenic mode of action. Puberty and its associated biological changes, for example, involve many biological processes that could lead to changes in susceptibility to the effects of some carcinogens, depending on their mode of action. The Agency is interested in identifying lifestages that may be particularly sensitive or refractory for carcinogenesis, and believes that the mode of action framework described in the Agency's *Guidelines for Carcinogen Risk Assessment* is an appropriate mechanism for elucidating these lifestages. For each additional mode of action evaluated, the various age groupings determined to be at differential risk may differ from those described in this Supplemental Guidance. For example, the age groupings selected for the age-dependent adjustments were initially selected based on the available data, i.e., for the laboratory animal age range representative of birth to < 2 years in humans. More limited data and information on human biology are being used to determine a science-informed policy regarding 2 to < 16 years. Data were not available to refine the latter age group. If more data become available regarding carcinogens with a mutagenic mode of action, consideration may be given to further refinement of these age groups.

Access to data and other information relating to the Cancer Guidelines (U.S. EPA, 2005) and this Supplemental Guidance will be through EPA's Risk Assessment Forum website, under Publications, Guidelines, Guidelines for Cancer Risk Assessment. The URL is http://www.epa.gov/cancerguidelines. The data and results of analyses are available in spreadsheets.

1. INTRODUCTION

Cancer risk to children in the context of the U.S. Environmental Protection Agency's cancer guidelines (U.S. EPA, 2005) includes both early-life exposures that may result in the occurrence of cancer during childhood and early-life exposures that may contribute to cancers later in life. The National Research Council (NRC, 1994) recommended that "EPA should assess risks to infants and children whenever it appears that their risks might be greater than those of adults." This document focuses on cancer risks from early-life exposure compared with those from exposures occurring later in life. Evaluating childhood cancer and childhood exposures resulting in cancer later in life are related, but separable, issues.

Historically, the focus on cancer has been as a disease associated with aging, resulting from extended exposure duration with prolonged latency periods before the cancers appear. Because much of cancer epidemiology addresses occupational exposures and because rodent cancer studies are designed to last approximately a lifetime (two years) beginning after sexual maturity, the cancer database used by EPA and other agencies for risk assessment focuses on adults. However, extensive literature demonstrates that exposures early in life (i.e., transplacental or *in utero*, early postnatal, lactational) in animals can result in the development of cancer (reviewed in Toth, 1968; Della Porta and Terracini, 1969; Druckery, 1973; Rice, 1979; Vesselinovitch et al., 1979; Rice and Ward, 1982; Vesselovitch et al., 1983; Anderson et al., 2000). Thus, one element in extending analyses to children is to evaluate the extent to which exposures early in life would alter the incidence of cancers observed later in life, compared with the incidence observed with adult-only exposures (Anderson et al., 2000; NRC, 1993).

The causes of cancer encompass a variety of possible risk factors, including genetic predisposition (Tomlinson et al., 1997), diet, lifestyle, associations with congenital malformations (Bosland, 1996), and exposure to biological and physical agents and chemicals in the environment. In some cases, tumors in adults and children have been compared (Anderson et al., 2000; Ginsberg et al., 2002). Children and adults generally develop the same spectrum of tumors when they have inherited gene and chromosomal mutations, such as Li-Fraumeni syndrome (Birch et al., 1998). With ionizing radiation, which operates through a mutagenic mode of action, both the young and the old develop many of the same tumors, with the difference being that children are more susceptible for a number of tumor types (NRC, 1990; U.S. EPA, 1994; UNSCEAR, 2000). Studies with anticancer drugs (cytotoxic and immunosuppressive) demonstrate a similar spectrum of tumors (Hale et al., 1999; Kushner et al., 1998; Larson et al., 1996; Nyandoto et al., 1998). Various viral infections, such as Epstein Barr and hepatitis B, lead to lymphoma and liver cancer, respectively, in both age groups (Lindahl et

al., 1974; Mahoney, 1999). These observations in humans indicate that the mode of action for these agents would be the same or similar for adults and children.

Although there are similarities between childhood and adult tumors, significant differences are also known to exist (Grufferman, 1998; Israel, 1995). Tumors of childhood generally consist more of embryonic cell tumors, while adults have more carcinomas. Leukemias, brain and other nervous system tumors, lymphomas (lymph node cancers), bone cancers, soft tissue sarcomas, kidney cancers, eye cancers, and adrenal gland cancers are the most common cancers of children, while skin, prostate, breast, lung, and colorectal cancers are the most common in adults (Ries et al., 1999; U. S. Cancer Statistics Working Group, 2002). Some tumors are unique to the young, including several with well established genetic bases, such as tumors of the kidney (Wilms' tumor) or eye (retinoblastoma) (Anderson et al., 2000; Israel, 1995).

The relative rarity in the incidence of childhood cancers and a lack of animal testing guidelines with perinatal[1] exposure impede a full assessment of children's cancer risks from exposure to chemicals in the environment. Unequivocal evidence of childhood cancer in humans occurring from chemical exposures is limited (Anderson et al., 2000). Established risk factors for the development of childhood cancer include radiation and certain pharmaceutical agents used in chemotherapy (Reise, 1999). There is some evidence in humans for adult tumors resulting from perinatal exposure. Pharmacological use of diethylstilbesterol (DES) during pregnancy to prevent miscarriages induced clear cell adenocarcinoma of the vagina in a few daughters exposed *in utero* though this tumor was not observed in exposed mothers (Hatch et al., 1998; Robboy et al., 1984; Vessey, 1989). In addition to the limited human data, there are examples of transplacental carcinogens in animal studies, such as recent studies with nickel and arsenic (Diwan et al., 1992; Waalkes et al., 2003), as well as studies suggesting that altered development can affect later susceptibility[2] to cancer induced by exposure to other chemicals (Anderson et al., 2000; Birnbaum and Fenton, 2003).

Infrequently, perinatal exposure in animals has been shown to induce tumors of different types than those observed with adult exposures. Studies with saccharin (Cohen et al., 1995; Whysner and Williams, 1996; IARC, 1999) and ascorbate (Cohen et al., 1998; Cohen et al., 1995; NTP, 1983) found cancer when exposures were initiated in the perinatal period. In

[1] Perinatal is defined as the time around birth and may include both prenatal (prior to birth) and postnatal (after birth) periods.

[2] Susceptibility is defined here as an increased likelihood of an adverse effect, often discussed in terms of relationship to a factor that can be used to describe a human subpopulation (e.g., lifestage, demographic feature, or genetic characteristic). The terms "susceptibility" and "sensitivity" are used with a variety of definitions in published literature making it essential that readers are aware of these differences in terminology across documents.

contrast, studies submitted to the Food and Drug Administration of approximately a dozen other food additives and colorings that were not adult carcinogens did not indicate cancer, even when perinatal exposures occurred (U.S. EPA, 1996). When observed, the differences between childhood and adult cancers suggest the importance of evaluating the impacts of maternal exposures during pregnancy as well as exposures to children (Anderson et al., 2000). The effects of maternal exposures and transplacental carcinogens require separate evaluation and are not quantitatively evaluated in the analysis presented below.

The limited human information described briefly above is supported by a number of animal bioassays that include both perinatal and adult exposures to chemicals. Standard animal bioassays generally begin dosing after the animals are 6-8 weeks old, when many organs and systems are almost fully developed, though substantial growth in body size continues thereafter (as more fully discussed in Hattis et al., 2005). The literature can be divided roughly into three types of exposure scenarios: those that include *repeated* exposures for the early postnatal to juvenile period, as compared with chronic later-life dosing; *lifetime* (i.e., combined perinatal and adult) exposure as compared with chronic later-life dosing; and those that include more *acute* exposures, such as a single intraperitoneal (ip) or subcutaneous injection, for both early-life and later-life dosing. In the early-life exposure studies that are available, perinatal exposure usually induces higher incidence of tumors later in life than the incidence seen in standard bioassays where adult animals only were exposed; some examples include diethylnitrosamine (DEN) (Peto et al., 1984), benzidine (Vesselinovitch et al., 1979), DDT (Vesselinovitch et al., 1979), and polybrominated biphenyls (PCBs) (Chhabra et al., 1993a). Reviews comparing early-life carcinogenesis bioassays with standard bioassays for a limited number of chemicals (McConnell, 1992; Miller et al., 2002; U.S. EPA, 1996) have concluded:

- The same tumor sites usually are observed following either perinatal or adult exposure.
- Perinatal exposure in conjunction with adult exposure usually increases the incidence of tumor bearing animals or reduces the latent period before tumors are observed.

There is limited evidence to inform the mode(s) of action leading to differences in tumor type and tumor incidence following early-life exposure and exposure later in life. Differences in the capacity to metabolize and clear chemicals at different ages can result in larger or smaller internal doses of the active agent(s), either increasing or decreasing risk (Ginsberg et al., 2002; Renwick, 1998). There is reason to surmise that some chemicals with a mutagenic mode of action, which would be expected to cause irreversible changes to DNA, would exhibit a greater effect in early-life versus later-life exposure. Several studies have shown increased susceptibility

of weanling animals to the formation of DNA adducts following exposure to vinyl chloride (Laib et al., 1989; Morinello et al., 2002a; Morinello et al., 2002b). Additionally, even though not used quantitatively in the analyses in this document, a recent analysis of *in vivo* transplacental micronucleus assays indicated that fetal tissues generally are more sensitive than maternal tissues for induction of micronuclei from mutagenic chemicals (Hayashi et al., 2000), providing qualitative support for the early-life susceptibility. Similarly, the neonatal mouse model for carcinogenesis, which uses two doses prior to weaning followed by observation of tumors at one year, shows carcinogenic responses for mutagenic agents (Flammang et al., 1997; McClain et al., 2001). These results are consistent with the current understanding of biological processes involved in carcinogenesis, which leads to a reasonable expectation that children can be more susceptible to carcinogenic agents than adults (Anderson et al., 2000; Birnbaum and Fenton, 2003; Ginsberg, 2003; Miller et al., 2002; Scheuplein et al., 2002). Some aspects potentially leading to childhood susceptibility include the following issues.

- More frequent cell division during development can result in enhanced fixation of mutations due to the reduced time available for repair of DNA lesions and clonal expansion of mutant cells gives a larger population of mutants (Slikker et al, 2004).
- Some embryonic cells, such as brain cells, lack key DNA repair enzymes.
- Some components of the immune system are not fully functional during development (Holladay and Smialowicz, 2000; Holsapple et al., 2003).
- Hormonal systems operate at different levels during different lifestages (Anderson et al., 2000).
- Induction of developmental abnormalities can result in a predisposition to carcinogenic effects later in life (Anderson et al., 2000; Birnbaum and Fenton, 2003; Fenton and Davis, 2002).

The methodology that has been generally used by the U.S. EPA to estimate cancer risk associated with oral exposures relies on estimation of the lifetime average daily dose, which can account for differences between adults and children with respect to exposure factors such as eating habits and body weight. However, susceptibility differences with respect to early lifestages are not taken into consideration because cancer slope factors[3] are based upon effects

[3] Cancer slope factor – An upper bound estimate of the increased cancer risk from a lifetime exposure to an agent. This estimate, usually expressed in units of proportion (of a population) affected per unit exposure (e.g., mg/kg-day or ug/m^3), is generally reserved for use in the low-dose region of the dose-response relationship. It is often the statistical upper bound on the potency and therefore the risk. “Upper bound” in this context is a plausible

observed following exposures to adult humans or sexually mature animals. Since a much larger database exists for chemicals inducing cancer in adult humans or sexually mature animals, it is necessary to determine whether adjustment of such adult-based cancer slope factors would be appropriate when assessing cancer risks associated with exposures early in life. The analysis undertaken here addresses this issue, focusing upon studies that define the potential duration and degree of increased susceptibility that may arise from childhood, defined as early-life (typically postnatal and juvenile animal) exposures. Some of these analyses, along with a more complete description of the procedures used, have been published (Barton et al., 2005). The analysis presented in this Supplemental Guidance and in the published article form the basis for developing Supplemental Guidance for evaluating cancer susceptibility associated with early-life exposures.

upper limit to the true probability.

2. PROCEDURES

This section describes the steps taken to assess potential susceptibility to early-life exposure to carcinogenic compounds compared with adult and whole-life exposure. The readily available literature was reviewed to identify animal studies that compared tumor incidence between early-life and adult-only exposures or between early-life-and-adult and adult-only exposures. Studies were categorized by length of exposure; those studies with quantitative information to estimate tumor incidence over time for early-life and adult exposures were identified. These studies provided the basis for quantitatively estimating the difference in susceptibility between early-life and adult exposures, as described below. Finally, summaries of available human data for radiation exposure were reviewed in the context of tumor incidence from early-life versus later-in-life exposure.

2.1. DATA SOURCES FOR ANIMAL STUDIES

Studies in the literature included in this analysis are those that report tumor response from experiments that included both early-life and adult exposure as separate experimental groups. Initial studies for consideration were identified through review articles and a search of the National Toxicology Program (NTP) database. Reviews of the literature regarding cancer susceptibility from early-life exposure in animals include McConnell (1992), Ginsberg (2003), Anderson et al. (2000), Miller et al. (2002) and U.S. EPA (1996). A literature search was conducted utilizing key words and MeSH headings (Medline) from studies identified in the available reviews. The list of chemicals included in this analysis for quantitative evaluation is shown in Table 1a and 1b.

Abstracts or papers were reviewed to determine if a study provided information that could be used for quantitative analysis. The criteria used to decide if a study could be included in the quantitative analysis were:

- Exposure groups at different post-natal ages in the same study or same laboratory, if not concurrent (to control for a large number of potential cross-laboratory experimental variables including pathological examinations),

- Same strain/species (to eliminate strain-specific responses confounding age-dependent responses),

- Approximately the same dose within the limits of diets and drinking water intakes that obviously can vary with age (to eliminate dose-dependent responses confounding age-dependent responses),

- Similar latency period following exposures of different ages (to control for confounding latency period for tumor expression with age-dependent responses), arising from sacrifice at >1 year for all groups exposed at different ages, where early-life exposure can occur up to about 7 weeks. Variations of around 10 to 20% in latency period are acceptable,

- Postnatal exposure for juvenile rats and mice at ages younger than the standard 6 to 8 week start for bioassays; prenatal (*in utero*) exposures are not part of the current analysis. Studies that have postnatal exposure were included (without adjustment) even if they also involved prenatal exposure,

- "Adult" rats and mice exposure beginning at approximately 6 to 8 weeks old or older, i.e. comparable to the age at initiation of a standard cancer bioassay (McConnell, 1992). Studies with animals only at young ages do not provide appropriate comparisons to evaluate age-dependency of response (e.g., the many neonatal mouse cancer studies). Studies in other species were used a supporting evidence, because they are relatively rare and the determination of the appropriate comparison ages across species is not simple, and

- Number of affected animals and total number of animals examined are available or reasonably reconstructed for control, young, and adult groups (i.e., studies reporting only percent response or not including a control group would be excluded unless a reasonable estimate of historical background for the strain was obtainable).

Tables 2 and 3 include information on the methods and results from the animal studies identified in Table 1b. Pertinent information on species, sex, dosing regimen, and tumor incidence is given. Additionally, the "Notes" column includes general information about the relationship between tumor incidence, animal age at first dosing, and sex. The data in Tables 2 and 3 were used for the calculations, described below, for estimating potentially increased cancer risk from early-life exposure.

The available literature includes a wide range of exposure scenarios. This range is due in part to the lack of a defined protocol for early-life testing and the difficulty of standardizing and administering doses preweaning. As noted previously, the literature can be divided roughly into three types of exposure scenarios: those that include repeated exposures for the early postnatal to juvenile period, as compared with chronic later-life dosing; lifetime (i.e., combined perinatal and adult) exposure as compared with chronic later-life dosing; and those that include more acute exposures, such as a single intraperitoneal (ip) or subcutaneous injection, for both early-life and later-life dosing. Table 2 includes the studies that had early postnatal to juvenile exposures, adult chronic exposures, and lifetime exposures. Table 3 includes studies with acute exposures. A discussion of the implications of the different exposure scenarios is included in Section 3.

Studies were identified for more than 50 chemicals not included in Tables 2 and 3 that demonstrated carcinogenesis following perinatal exposure, but did not directly compare exposures at different ages. A large number of studies address *in utero* exposures only. More than 100 chemicals (with both negative and positive findings) have been studied in the neonatal mouse assay, but this assay does not have a comparable adult exposure (Flammang et al., 1997; McClain et al., 2001; Fujii, 1991). Studies across laboratories often varied in their use of animal strains (e.g., for AZT studies, Diwan et al., 1999 used CD-1 mice, while NTP, 1999 used $B6C3F_1$ mice). Studies of tamoxifen use two Wistar-derived strains and had very different periods for tumor expression, i.e., sacrifice at 20 months for adult-exposed rats and natural death up to 35 months for juvenile-exposed rats, with uterine tumors observed in animals dying after 22 months (Carthew et al., 2000; Carthew et al., 1996; Carthew et al., 1995). Due to these factors, the chemicals that belong to this group were not evaluated quantitatively. In addition, there were studies assessing radiation in animals (Covelli et al., 1984; Di et al., 1990; Sasaki et al., 1978). The radiation data were not analyzed in depth, in part because there are recognized differences in toxicokinetics and toxicodynamics between radiation and chemicals with a mutagenic mode of action for carcinogenesis. Even though the data on A-bomb survivors provide information for many different cancer sites in humans with a single exposure involving all ages, a number of national and international committees of experts have analyzed and modeled these data to develop risk estimates for various specific applications. Furthermore, lack of uniformity regarding radiation doses, gestational age at exposure, and the animal strains used make it difficult to make comparisons across studies (Preston et al., 2000).

2.2. EVALUATING THE MODE OF ACTION OF CARCINOGENS

Evaluation of the mode of action of a carcinogen was based upon a weight-of-evidence approach. Multiple modes of action are associated with the chemicals in this database, but a number are associated with mutagenicity (i.e., benzo(a)pyrene, benzidine, dibenzanthracene, diethylnitrosamine, dimethylbenz(a)anthracene, dimethylnitrosamine, ethylnitrosourea, 3-methylcholanthrene, methylnitrosourea, safrole, urethane, and vinyl chloride). Determination of carcinogens that are operating by a mutagenic mode of action entails evaluation of short-term testing results for genetic endpoints, metabolic profiles, physicochemical properties, and structure-activity relationship (SAR) analyses in a weight-of-evidence approach (Dearfield et al., 1991; U.S. EPA, 1986, 1991; Waters et al., 1999), as has been done for several chemicals (e.g., Dearfield et al., 1999; McCarroll et al., 2002; U.S. EPA, 2000a). Key data for a mutagenic mode of action may be evidence that the carcinogen or a metabolite is DNA reactive and/or has the ability to bind to DNA. Also, such carcinogens usually produce positive effects in multiple test

systems for different genetic endpoints, particularly gene mutations and structural chromosome aberrations, and in tests performed *in vivo* which generally are supported by positive tests *in vitro*. Additionally, carcinogens may be identified as operating via a mutagenic mode of action if they have similar properties and SAR to established mutagenic mode of action.

2.3. QUANTITATIVE METHODS

To estimate the potential difference in susceptibility between early-life and adult exposure, we calculated the estimated ratio of the cancer potency from early-life exposure compared to the estimated cancer potency from adult exposure. The cancer potency was estimated from a one-hit model, or a restricted form of the Weibull model, which is commonly used to estimate cumulative incidence for tumor onset. The general form of the equation is:

P(dose) = 1-[1-P(0)]exp(-cancer potency*dose)

The ratio of juvenile to adult cancer potencies were calculated by fitting this model to the data for each age group. The model fit depended upon the design of the experiment that generated the data. Two designs should be handled separately: experiments in which animals are exposed either as juveniles or as adults (with either a single or multiple dose in each period), and experiments in which exposure begins either in the juvenile or in the adult period, but once begun, continues through life.

For the first case, the model equations are:

$$P_A = P_0 + (1 - P_0)(1 - e^{-m_A \delta_A}) \qquad (1)$$
$$P_J = P_0 + (1 - P_0)\left(1 - e^{-m_A e^{\lambda} \delta_J}\right)$$

where:

subscripts *A* and *J* refer to the adult and juvenile period, respectively,
λ is the natural logarithm of the juvenile:adult cancer potency ratio,
P_0 is the fraction of control animals with the particular tumor type being modeled,
P_x is the fraction of animals exposed in age period *x* with the tumor,
m_A is the rate of accumulation of "hits" per unit of time for adults, i.e., the cancer potency, and
δ_x is the duration or number of exposures during age period *x*.

For a substantial number of data sets (acute exposures), $\delta_J = \delta_A = 1$. We are interested in

determining λ, which is the logarithm of the estimated ratio of juvenile to adult cancer potencies, a measure of potential susceptibility for early-life exposure.

For the second kind of design, the model equations should take into account that exposures that were initiated in the juvenile period continue through the adult period. The model equations for the fraction of animals exposed only as adults with tumors in this design are the same as in the first design, but the fraction of animals whose first exposure occurred in the juvenile period is:

$$P_J = P_0 + (1 + P_0)\left(1 - e^{-m_A e^{\lambda}(\delta_J - \delta_A) - m_A \delta_A}\right) \quad (2)$$

All symbols in (eq. 2) have the same interpretation as their counterparts in (eq. 1), but now δ_J includes the duration of exposure during the juvenile period as well as the subsequent adult period.

Parameters in these models were estimated using Bayesian methods (see, for example, Carlin and Louis, 2000), and all inferences about the ratios were based on the marginal posterior distribution of λ. Some of these analyses, including a more complete description of the procedures (including the potential effect of alternative Bayesian priors that have been examined) have been published (Barton et al., 2005). The data for estimating each ratio were in the form of numbers of animals tested and number affected for each of control, juvenile-exposed, and adult-exposed animals, and duration of exposure for each of the juvenile-exposed and adult-exposed groups. A few data sets had separate control groups for the juvenile-exposed and adult-exposed groups, and equations 1 and 2 were modified accordingly. The likelihood for the parameters in the model was the product of three (or four, if there were two control groups) binomial probabilities: for the number of animals with tumors in the control group(s), for the juvenile-exposed group, and for the adult-exposed group. The prior for P_0 (the fraction of control animals with a particular tumor) was right triangular (right angle at the origin), based on the assumption that control incidences should be relatively low. (The base of the distribution is one, as P_0 can not exceed one. As this is a probability distribution, the area of the triangle is one. Therefore, its height at the origin must be 2.) The effect of exposure in adults is quantified by the extra risk, Q, where the probability that an animal has a tumor is $P_0 + (1 - P_0)Q$. So, from equations 1, $Q = 1 - e^{-m_A \delta_A}$, Q was given a uniform prior on the interval (0,1), reflecting total ignorance about the extra risk of adult exposure. Finally, the prior for λ was Gaussian with mean 0 (corresponding to a median or geometric mean ratio of one) and standard deviation 3. The prior for the log ratio of juvenile to adult cancer potency has some influence over the posterior estimates for the ratio of juvenile to adult potency. The magnitude of that influence depends on

the amount of support in the data for different values of the log ratio. The prior also effectively downweights extremely large or small values for the juvenile to adult potency ratio. Three priors for the standard deviation were evaluated (Barton et al., 2005, see Appendix), with the intent of finding the largest prior, i.e., one that would contain the least informative assumption for the prior. A standard deviation of 9 was tried, but some of the intervals would not converge. A standard deviation of 3 worked well, allowed ratio estimates to be derived, with all of the data of interest. An intermediate value of 6 was also examined to ascertain if a less informative prior could be used. While the intervals converged, a sensitivity analysis showed that this value for the standard deviation resulted in sufficient down-weighting of the ratios with limited information that these data would not influence the result. This was considered an unreasonable bias, so a standard deviation of 3 was used for the further analyses. A further discussion of these analyses can be found in Barton et al. (2005).

The posterior distribution for the unknown parameters in these models is the product of the likelihood from the data and the priors (the "unnormalized" prior), divided by a normalization constant that is the integral of the unnormalized prior over the ranges of all the parameters. This normalization constant was computed using numerical integration, as were posterior means and variances and marginal posterior quantiles for the log-ratio λ. All numerical computations were carried out in the R statistical programming language (version 1.8.1; R Development Core Team, 2003).

This method produced a posterior mean ratio of the early-life to adult cancer potency, which is an estimate of the potential susceptibility of early-life exposure to carcinogens. If the ratio was greater than one, this indicated that the experiment found that there was greater susceptibility from early-life exposure. If the ratio was less than one, this indicated that the experiment found that there was less susceptibility from early-life exposure. Summaries of the individual ratios from each of the dose groups from the different experiments for different groupings were also calculated (for example for all acute exposures of chemicals that are carcinogenic by a mutagenic mode of action). The summary ratios were constructed from the individual ratios within a group, by variance-weighting the means of each ratio. The individual, posterior means were weighted by using reciprocals of their posterior variance. This weighting procedure is commonly used because it gives greater weight to those studies for which the variances, i.e., the uncertainties, are smaller. Because the ratios were calculated as log ratios (see eq. 1), exponentiating the resulting inverse-variance-weighted mean yielded inverse-variance-weighted geometric means of ratios.

2.4. IONIZING RADIATION

A supporting role was assigned to the available human radiation data, where cancer incidence in adults who were children at the time of the atomic bomb (A-bomb) exposure was compared with cancer incidence in adults who were older at the time of exposure. Although there are recognized differences in toxicokinetics and toxicodynamics between radiation and chemical carcinogens with a mutagenic mode of action, the data on A-bomb survivors provide information for many different cancer sites in humans with a single exposure involving all ages. In addition to the richness of the data, a number of national and international committees of experts have analyzed and modeled these data to develop risk estimates for various specific applications.

The report of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 2000, with Scientific Annexes) lists more than 80 studies, in addition to the reports of the Japanese A-bomb survivors, in which at least one type of cancer was measured in humans who were exposed either intentionally or accidentally to some form of ionizing radiation. However only the A-bomb survivor reports have relevant information on incidence of early-life exposures. One of the more recent papers cited in the UNSCEAR report, by Thompson et al. (1994), contains detailed data on the incidence of 21 different cancers in 37,270 exposed A-bomb survivors (42,702 unexposed). Also, EPA has used data from the A-bomb survivors to develop age-specific relative risk coefficients using various methods for transporting the risk from the Japanese population to the U.S. population (U.S. EPA, 1994). It is beyond the scope of this effort to present all of the radiation data or a discussion of the various analyses and modeling efforts. Rather, information relevant to comparing cancer risks from juvenile versus adult exposure from UNSCEAR (2000) and U.S. EPA (1994; 1999) is presented as representative findings to determine whether the radiation data are similar qualitatively to the chemical findings. More detailed data on the A-bomb survivors can be found in Delongchamp et al. (1997) and Preston et al. (2000).

As previously noted, several studies have assessed radiation in animal studies (Covelli et al., 1984; Di et al., 1990; Sasaki et al., 1978). However, lack of uniformity regarding radiation doses, gestational age at exposure, and the animal strains used make it difficult to compare the experimental data on cancer induction after prenatal irradiation (Preston et al., 2000).

3. RESULTS

3.1. QUALITATIVE EVALUATION OF THE DATABASE

The question addressed in this analysis was whether, and how, available quantitative scientific data could inform risk assessment policy choices for adjusting cancer slope factors when they are used in the assessment of cancer risk from childhood exposure. Cancer slope factors are, with few exceptions, based on adult human epidemiology or standard chronic adult rodent bioassays, which do not address the impacts of early-life exposures. Thus, the critical data are either human epidemiological data on childhood exposures resulting in adult cancer or research studies with rodents involving early postnatal exposures. The major human data available are from radiation exposures (studies summarized in Tables 9-11), with very limited data available for humans exposed during childhood to chemicals (reviewed in Anderson et al., 2000; Miller et al., 2002).

A review of the literature identified several hundred references reporting more than 50 chemicals that have been shown to be able to cause cancer following perinatal exposure (Table 1a) (reviewed in Toth, 1968; Della Porta and Terracini, 1969; Druckery, 1973, Rice, 1979; Vesselinovitch et al., 1979; Rice and Ward, 1982; Vesselovitch et al.; 1983; Fujii, 1991; Anderson et al., 2000). Studies (or groups of studies from a single laboratory on a given chemical) that directly provided quantitative data on carcinogenesis following early postnatal exposures and adult exposures to chemicals in animals were identified for 18 chemicals, listed in Table 1b, 2, and 3. Of the identified studies, there were 11 chemicals involving repeated exposures during early postnatal and adult lifestages (Table 1b) and 8 chemicals using acute exposures (typically single doses) at different ages (Table 1b). Some of the studies evaluated single tissues or organs for tumors (e.g., only liver), while others evaluated multiple tissues and organs (Tables 2 and 3). Mice, rats, or both species and sometimes multiple strains were tested. These studies serve as the basis for the quantitative analyses presented later in the results.

In addition to the studies identified in Table 1b, studies were identified with early postnatal and early-life exposures that were evaluated qualitatively but not quantitatively. Some of these studies are notable and provide important supporting information. Two recent studies used transgenic mouse models for human tumors. Increased multiplicity of colon tumors was observed following earlier versus later azoxymethane exposures (Paulsen et al., 2003). Shortened mammary tumor latency following estradiol exposure occurred when exposures occurred between 8 and 18 weeks as opposed to earlier or later, which is generally consistent with the incidence results analyzed for DMBA (Yang et al., 2003). Several notable examples exist of developmental windows leading to cancer susceptibilities that were not observable in

adults. Several potent estrogenic chemicals including DES, tamoxifen, and genistein produce uterine tumors with early postnatal exposures of mice, though there also appear to be strain-dependent differences in the tumor sites in adult mice (Gass et al., 1964; Greenman et al., 1990; Newbold et al., 1990, 1997, 1998, 2001). Developmental susceptibilities are believed to play a key role in effects observed with saccharin (Cohen et al., 1995; Whysner and Williams, 1996) and ascorbate (Cohen et al., 1998; NTP, 1983), with bladder tumors arising when early-life exposures occurred. Studies with several species, including rat, mouse, and opossum, indicate that nervous systems tumors associated with exposures to ENU and several other chemicals appear to be highly dependent upon exposures occurring within certain windows, particularly prenatal ones (Rice, 1979; Rice and Ward, 1982; Jurgelski et al., 1979).

Analyses of the difference in cancer risk from exposures during different lifetime periods ideally should address both the period of potential susceptibility and the magnitude of the susceptibility. Available studies used a variety of study designs (see Tables 2 and 3), which can be valuable because they provide different information (Figure 1). However, variations in study design can result in a lack of comparability across chemicals, and can limit information on the consistency of effects with different chemicals acting through different modes of action. The acute dosing (largely single dose) studies (Table 3) are valuable because they involve identical exposures with explicitly defined doses and time periods demonstrating that differential tumor incidences arise exclusively from age-dependent susceptibility. These studies address both the period and magnitude of susceptibility. They were not as appropriate for quantitative adjustments for the cancer potency estimates because of their limitations, including that most used subcutaneous or ip injection that historically have not been considered quantitatively relevant routes of environmental exposure for human cancer risk assessment by EPA, and that these routes of exposure are expected to have only partial or a complete absence of first pass metabolism that is likely to affect potency estimates.

The repeated dosing studies with exposures during early postnatal or adult lifetime provide useful information on the relative impact of repeated exposures at different lifestages and may be more likely to have exposure occur during a window of susceptibility, if there is one. One notable difference in study designs was that studies with repeated early postnatal exposure were included in the analysis even if they also involved earlier maternal and/or prenatal exposure, while studies addressing only prenatal exposure were not otherwise a part of this analysis. Another notable difference among studies involved the tissues that were evaluated for tumors: some studies focused on a single tissue, particularly liver, while others evaluated multiple tissues.

Comparisons within a single repeated dosing study may have limitations for evaluating

differential susceptibility because exposures to the chemical can differ during the different lifestages, particularly when dietary or drinking water exposures are involved. A notable example is the PCB study (Chhabra et al., 1993a), in which mobilization of such lipid-soluble chemicals into mother's milk would be expected to result in infants receiving much larger exposures than other lifestages. While lactational transfer is just as relevant to human nursing offspring, this difference in exposure obscures the extent to which the early lifestage is quantitatively more susceptible (i.e., part of the increased early-life cancer risk arises from higher exposure than during the adult period). Maternal metabolism of compounds such as diphenylhydantoin (DPH) (Chhabra et al., 1993b) also may result in lower exposure during lactation, potentially underestimating the early-lifestage risk, if the parent compound is the active form of the chemical. Similar issues exist due to normal age-dependent changes in food and water consumption. Ascribing differential effects observed in animal studies solely to lifestage susceptibility must be done carefully as there may also be differences in the exposures. There are substantial and clear benefits, therefore, from experimental consistency when comparisons are made directly within a study (e.g., same species and strain, consistent pathological evaluation).

One issue to note is the rationale for the organization of the available data. It was observed that the results across a broad range of chemicals with a variety of modes of action were somewhat variable. Therefore, consistent with the approach of the EPA cancer guidelines (U.S. EPA, 2005), an approach based on mode of action appeared to be a common framework for analysis. Variability in lifestage-dependent susceptibility and susceptibility across a range of modes of action was further supported by theoretical analyses using multistage and two-stage models of carcinogenesis (Goddard and Krewski, 1995; Murdoch et al., 1992).

3.2. QUANTITATIVE EVALUATION OF THE DATABASE

As described in the Section 2.3, the potential difference in susceptibility between early-life and adult exposure was calculated as the estimated ratio of cancer potency from early-life exposure over the cancer potency from adult exposure. Tables 4-7 present the results of the quantitative analysis using the studies that were determined qualitatively to have appropriate study designs (Tables 2 and 3) containing sufficient information to analyze. Based on the studies available, the calculations were organized into four tables: (1) compounds acting through a primarily mutagenic mode of action, where the compound was administered by a chronic dosing regimen to adults and repeated dosing in the early postnatal period (Table 4); (2) compounds acting through a primarily nonmutagenic mode of action, where the compound was administered by a chronic dosing regimen to adults and repeated dosing in the early postnatal period (Table 5);

(3) compounds acting through a primarily mutagenic mode of action, where the compounds were administered by an acute dosing regimen (Table 6); and (4) compounds acting primarily through either a mutagenic or nonmutagenic mode of action with chronic adult dosing and repeated early postnatal dosing (Table 7). In these tables, the 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses. The results are discussed below, followed by a description of results from analyses of studies of humans exposed to radiation.

3.2.1. Carcinogens with a Mutagenic Mode of Action

The most informative database on early-lifestage susceptibility exists for chemicals with a well-accepted mutagenic mode of action (e.g., diethylnitrosamine, vinyl chloride). This database includes both single-dose studies and repeated-dose studies involving periods of postnatal and/or chronic exposure. These studies help define the periods of increased vulnerability and the magnitude of the susceptibility. The acute dosing studies demonstrate that the age-dependent responses are not due to differences in exposure, because these studies explicitly control the exposure.

3.2.1.1. *Early Postnatal, Juvenile, and Adult Repeated Dosing Studies of Chemicals with a Mutagenic Mode of Action*

Studies comparing repeated dosing for early-life, adult, or lifetime exposures exist for six carcinogens with a mutagenic mode of action [benzidine, diethylnitrosamine (DEN), 3-methylcholanthrene, safrole, urethane, and vinyl chloride]; DEN also had acute dosing studies. Lifetime (i.e., combined juvenile and adult) compared to adult exposure studies were analyzed for DEN, safrole, and urethane, while studies comparing juvenile with adult exposures were analyzed for benzidine, 3-methylcholanthrene, safrole, and vinyl chloride. These chemicals all require metabolic activation to the active carcinogenic form. Analysis of the tumors arising per unit time of exposure found that juvenile exposures with each chemical could be more effective than adult exposures were at inducing tumors (Tables 4 and 7; Figure 2, a graphic representation of the posterior, unweighted geometric means and their 95% confidence intervals, for the ratios of juvenile to adult cancer potency for carcinogens acting through a mutagenic mode of action). The weighted geometric mean for repeat and lifetime exposures is 10.4; for acute exposures the weighted geometric mean value is 1.5. For benzidine and safrole, there was a notable sex difference, with high liver tumor incidence observed for early postnatal exposures of male, but not female, mice. For both the acute and the repeated/lifetime data, the 95th percentile of the individual, unweighted geometric means is above 10 (Figure 2).

This analysis focused upon the duration of exposure as a surrogate for dose, essentially assuming that the doses animals received during the different periods of these studies were similar. This assumption is a limitation of the analysis because these studies involved exposures via lactation (i.e., dosing the mother prior to weaning), drinking water, diet, or inhalation, which have the potential to deliver different doses at different lifestages. However, the range of the magnitudes of the tumor incidence ratios of juvenile to adult exposures is similar (Table 8) for the repeated dosing studies (0.12 – 111, weighted geometric mean 10.5, 42% of ratios greater than 1), lifetime dosing studies (0.18 – 79, weighted geometric mean 8.7, 67% of ratios greater than 1), and acute dosing studies (0.01 – 178, weighted geometric mean 1.5, 55% of ratios greater than 1), suggesting that these differences in dosing are not the sole determinant of the increased incidence of early tumors, i.e., uncertainty and variability remain. Because these comparisons include different chemicals with different tissue specificities, it may be informative to consider liver as a target organ affected by all of these chemicals. The range of the magnitudes of the liver tumor incidence ratios of juvenile to adult exposures is similar for the repeated dosing studies (0.12 – 111, weighted geometric mean 41.8, 86% of ratios greater than 1, Table 4), lifetime dosing studies (0.47 – 79, weighted geometric mean 14.9, 80% of ratios greater than 1, Table 7), and acute dosing studies (0.1 – 40, weighted geometric mean 8.1, 77% of ratios greater than 1, Table 8). Thus, the repeated dose studies support the concept that early-lifestage exposure to carcinogenic chemicals with a mutagenic mode of action would lead to an increased tumor incidence compared with adult exposures of a similar duration and dose.

3.2.1.2. *Acute Dosing Studies of Chemicals with a Mutagenic Mode of Action*

Acute dosing studies are available for eight carcinogens with a mutagenic mode of action that were administered to mice or rats [benzo[a]pyrene (BaP), dibenzanthracene (DBA), Diethylnitrosamine (DEN), dimethylbenzanthracene (DMBA), dimethylnitrosamine (DMN), ethylnitrosourea (ENU), methylnitrosourea (NMU), and urethane (also known as ethyl carbamate)] (Table 1b). Except for ENU and NMU, these compounds require metabolic activation to their active carcinogenic forms. These acute dosing studies generally compared a single exposure during the first few weeks of life with the identical or similar exposure in young adult animals (Tables 3 and 6). Many of these studies compared exposures during the preweaning period (i.e., approximately day 21 for rats and mice) with effects around week 6, which is approximately the age at which typical chronic bioassays begin dosing animals. These studies largely were by subcutaneous or ip injection, which historically have not been considered quantitatively relevant routes of environmental exposure for human cancer risk assessment by EPA. For purposes of comparing age-dependent susceptibilities to tumor development, these

data are highly relevant. The injection route typically alters the pharmacokinetic time courses of the parent compound and the metabolites compared with oral or other exposures due to altered kinetics of absorption and metabolism. However, for these compounds and the systemic organ effects observed, there are several pharmacokinetic reasons to believe that the age-dependent trends would be similar with other routes of exposure. These compounds are expected to be reasonably well absorbed orally, comparable with injection routes, and largely require metabolic activation, so partial or complete absence of first pass metabolism in the injection studies would be similar to or underestimate metabolic activation when compared with oral exposure.

The early exposures often resulted in higher incidence of tumors than later exposures, with increased early susceptibilities up to 178-fold (unweighted ratios in Table 6 range from 0.011 to 178, with a weighted geometric mean of 1.5, and 55% of ratios greater than 1, Figure 2, Table 8). Examples of the general age-dependent decline in susceptibility of tumor response include BaP (liver tumors), DEN (liver tumors), ENU (liver and nervous system tumors), and urethane (liver and lung tumors). While generally the Day 1 and Day 15 time points were higher than later time points, in several cases similar tumor incidence was observed at both these early times (e.g., ENU-induced kidney tumors, Tables 6 and 8).

While the degree of susceptibility generally declines during the early postnatal period through puberty into early adulthood, there are exceptions due perhaps to pubertal periods of tissue development (e.g., mammary tissues) or very early development of xenobiotic metabolizing enzymes. One such exception was the increased incidence of mammary tumors in 5-8 week old rats given DMBA, compared with older or younger rats (Meranze et al., 1969; Russo et al., 1979). Meranze et al. (1969) reported 8% mammary tumors following a single dose of DMBA at less than two weeks, 56% if given once to animals between 5 and 8 weeks old, and 15% when given once to 26 week old rats. Thus, a ratio of 7.1 is obtained when comparing susceptibilities of 5–8 week and 26-week-old rats (Table 6) compared to a ratio of 0.2 when comparing the exposure at 2 weeks versus 26 weeks. A similar effect was observed by Russo et al. (1979); see Table 3. This observation corresponds well with pubertal development of the mammary tissue, with ovarian function commencing between 3 and 4 weeks (after the < 2 week time point in the Meranze et al., 1969 study), and mammary ductal growth and branching occurring such that it is approximately two-thirds complete by week 5, consistent with the 5–8 week susceptible period of Meranze et al. (Silberstein, 2001). While this differs from the general trend previously discussed, it indicates susceptibility later in the juvenile period rather than earlier. Another example of deviation from the general trend toward an age-dependent decline is DEN-induced lung tumors that were somewhat lower in incidence following exposure on day 1 than observed for the day 15 or day 42 exposures (Vesselinovitch et al., 1975) (Tables 3 and 6).

There are substantial differences in the early-life susceptibility of different tissues observed in the acute studies (Table 8). It should be noted that the target tissues vary with chemical, so the number of chemicals for which data are available varies for each tissue. Several tissues have weighted geometric mean ratios of greater than 1 including kidney, leukemia, liver, lymph, mammary, nerve, reticular tissue, thymic lymphoma, and uterus/vagina. Some of these, such as the nerve and mammary tumors, appear to have a very specific window of susceptibility, as noted above, and the ratios were much higher if the exposure occurred during this window. Tissues with weighted mean ratios less than 1 include forestomach, harderian gland, ovaries, and thyroid. Lung has a weighted geometric mean of 1. Many of the studies produced very high lung tumor responses regardless of age, so the results are difficult to interpret, as illustrated by the dose-response data with urethane in Rogers (1951) in which the increased early susceptibility is only apparent when the dose is low. The large numbers of studies with high lung tumor responses at all ages contribute to the differences in the weighted geometric means for the acute and for the repeated dosing studies.

Overall, the acute dosing studies support the concept that early-lifestage exposure to carcinogenic chemicals with a mutagenic mode of action would lead to an increased incidence of tumors compared with adult exposures of a similar dose and duration. These studies generally use the same dose and duration at all ages, and thus do not have the type of issues discussed for the repeated dosing studies. On the other hand, the acute dosing studies have limitations that were sufficient to decide that they should not be included in the quantitative adjustment of cancer potency. First, as mentioned in the previous paragraph, the large number of studies of lung tumors with almost 100% response observed at all doses and all ages would significantly bias the median ratio toward unity for a reason based on study design rather than biology. Second, cancer potency estimates are usually derived from chronic exposures. Therefore, any adjustment to those potencies should be, if possible, from similar exposures. Third, most exposures of concern to the Agency are from repeated or chronic exposures rather than acute exposures. Finally, many of the acute studies used ip exposures, which is not the usual route of exposure for environmental chemicals. Thus, the repeated and lifetime studies are more appropriate for the purpose of this analysis.

3.2.2. Carcinogens With Modes of Action Other Than Mutagenicity

Studies comparing tumors observed at the same sites following early postnatal and chronic adult exposures in a single protocol were available for six chemicals that do not act through a mutagenic mode of action [amitrole, dichlorodiphenyltrichloroethane (DDT), dieldrin, ethylene thiourea (ETU), diphenylhydantoin (DPH), polybrominated biphenyls (PBB)] (Table 5).

These chemicals cause tumors through several different, not necessarily well defined, modes of action. For example, thyroid hormone disruption by ETU causes thyroid tumors; some PBBs act through aryl hydrocarbon (Ah) receptors, while others are phenobarbital-like pleiotrophic inducers of liver enzymes and liver tumors. Three of these studies evaluated only mouse liver tumors (amitrole, DDT, dieldrin), while the other three evaluated a large number of tissues in both mice and rats (ETU, DPH, PBB). These studies generally included a combined perinatal and adult exposure as well as the separate perinatal or adult-only groups. It should be noted that no acute perinatal dosing studies of carcinogenesis were identified for these agents; such protocols are generally considered largely non-responsive for modes of action other than mutagenicity and potent estrogenicity (e.g., DES).

For five chemicals (amitrole, DDT, dieldrin, PBB and DPH), the same tumors were observed from early and/or adult exposures, though the studies for amitrole, DDT, and dieldrin only evaluates the animals for liver tumors. With ETU, no tumors in mice or rats were observed following perinatal exposure alone (except a small, not-statistically-significant increase in male rat thyroid tumors), while thyroid tumors were observed in adult rats and thyroid, liver, and pituitary tumors in adult mice. Analysis of the incidence of tumors per time of exposure shows early-lifestage susceptibilities. The range of the magnitudes of the tumor incidence ratios of juvenile to adult exposures is similar for the repeated dosing studies (0.06–13.3, weighted geometric mean 2.2, 27% of ratios greater than 1, Tables 5 and 8) and lifetime dosing studies (0.15–36, weighted geometric mean 3.4, 21% of ratios greater than 1, Tables 7 and 8). These ranges and means are similar to those for chemicals with a mutagenic mode of action, though the means and maximums are somewhat lower. Again, liver tumors are common to these chemicals. The range of the magnitudes of liver tumor incidence ratios of juvenile to adult exposures also is similar for the repeated dosing studies (0.06–13.3, weighted geometric mean 2.6, 43% of ratios greater than 1, Tables 5 and 8) and lifetime dosing studies (0.15–36, weighted geometric mean 5.8, 33% of ratios greater than 1, Tables 7 and 8).

The major factor that complicates the interpretation of the results is that these studies, except with DDT and dieldrin, involved dietary feeding initially to the mother, which potentially could increase or decrease the dose received by the pups. Due to the maternal dosing during pregnancy and lactation, the extent to which offspring received similar doses during different early and adult lifestages is particularly uncertain for DPH, ETU, and PBBs. Oral gavage doses in young animals were selected to approximate the average daily dose in adult dietary studies based on standard estimates of feed consumption in the studies with DDT and dieldrin, while the amitrole study involved dietary feeding postnatally to the mother so the young were dosed via lactation. In addition, DDT, dieldrin, and some PBBs are more persistent in the body than are

most chemicals, leading to a prolonged exposure even following limited dosing. Thus, these studies provide evidence that early lifestages can be more susceptible to exposures to chemicals causing cancer through a variety of modes of action other than mutagenicity. However, the studies with ethylene thiourea, which acts via thyroid disruption, indicate that this is not necessarily the case for all modes of action.

3.2.3. Ionizing Radiation

As mentioned previously, the UNSCEAR, Annex I (2000) includes information derived from a wide range of both intentional (generally diagnostic or therapeutic medical) and accidental radiation exposures. Only information derived from the Japanese population (referred to as the Life Span Study in the UNSCEAR Annex I) is presented here. A statistically significant excess cancer mortality associated with radiation has been found among the bomb survivors for the following types of cancer: esophagus, stomach, colon, liver, lung, bone and connective tissue, skin, breast, urinary tract, and leukemia. Tables 9 and 10 are extracted from the tables in UNSCEAR, Annex I. The excess relative risk (ERR) is the increased cancer rate relative to an unexposed population; an ERR of 1 corresponds to a doubling of the cancer rate. Because of the low numbers of cancers in individual sites within narrow age groups, the ERRs for the various solid tumors and leukemia were presented only as less than or greater than 20 years of age at the time of exposure. The larger number of thyroid tumors enable a more detailed breakout shown in Table 10. Most sites show greater risks in the younger than in the older ages.

The U.S. EPA (1994) document presents a methodology for estimation of cancer risks in the U.S. population due to low-LET (linear energy transfer) radiation exposures using data from the Atomic Bomb Survivor Study (ABSS) as well as from selected medical exposures. The report developed mortality risk coefficients using several models that took into account age and gender dependence of dosimetry, radiogenic risk, and competing causes of death as well as transporting of risks across populations. The risk projections were updated using more recent vital statistics in a report that also included an uncertainty analysis (U.S. EPA, 1999). Details of the derivation of these coefficients are available at http://www.epa.gov/radiation/docs/rad_risk.pdf .

Table 11 contains the calculated age-specific risk coefficients derived from the application of the various models to the ABSS data. For most of the sites in the table, the risk coefficients are higher in the earlier age groups; liver, bone, skin, and kidney coefficients are age-independent and only esophageal cancer coefficients increase with increasing age. Also of note is that the coefficients generally are higher for females. Similar to the information from the UNSCEAR (2000) Annex, most sites show greater risks in the younger ages than the older ages.

However, a comparison of the two tables seems to show reversal of risks for some sites as a function of age at exposure. While the high sampling variability in the epidemiological data for some ages may contribute to this apparent reversal, the choice of risk models and associated parameters also is a factor.

4. DISCUSSION

The challenge for this analysis was how to use the existing, but limited, scientific database on early postnatal and juvenile exposures to carcinogens to inform a science policy decision on whether, and if so how, to assess the risk from childhood exposures to chemicals for which we have evidence of carcinogenicity only in adult humans or sexually mature laboratory animals. The database overall is of limited size (particularly compared with the number of chemicals that have been studied in adult occupational epidemiological studies or chronic bioassays). The majority of the human data involves exposures to ionizing radiation or DES (Anderson et al., 2000). More than 50 chemicals have been demonstrated to cause cancer following perinatal exposures in animals (without adult exposures), but only a subset of the chemicals have comparative studies across ages. The comparative experimental studies used 18 chemicals, 12 of which had mutagenic modes of action and 6 of which had data from repeated or lifetime exposures. Other analyses of similar data have found similar results (Hattis et al. 2005), but have focused on other aspects of the data, e.g., gender differences.

Previously published or internal U.S. EPA analyses have concluded that the standard animal bioassay protocols usually do not miss chemicals that would have been identified as carcinogens if perinatal exposures had been undertaken (McConnell, 1992; Miller et al., 2002; U.S. EPA, 1996). Given the increased complexity and costs of chronic bioassays with perinatal exposures, a limited number of such studies have been performed. However, these are the studies that largely constitute the available database for this analysis. In addition to the chronic bioassays with perinatal exposures, there are studies with acute dosing at different lifestages and a large number of studies with perinatal exposures without a directly comparative adult study.

Two other kinds of information can contribute toward developing a scientifically informed policy: theoretical analyses and analyses of stop studies.[4] Theoretical analyses suggest that the differential susceptibility would depend in part on the mode of action (i.e., at what step in the cancer process(s) the chemical was acting) and that the use of the average daily exposure prorated over a lifetime may underestimate or overestimate the cancer risk when exposures are time-dependent (Goddard and Krewski, 1995; Murdoch et al., 1992). Evidence for old-age-dependent promotion of basophilic foci in rats by peroxisome proliferators appears to provide a concrete example consistent with these theoretical analyses (Cattley et al., 1991; Kraupp-Grasl et al., 1991). The stop studies performed by the National Toxicology Program began exposure at the standard post-weaning age, but stopped exposure after varying periods of months. Other groups of animals were exposed for a full two years; all animals were evaluated

[4] Stop studies are studies in which exposure is halted after a predetermined period.

for tumors at the end of two years regardless of the duration of exposure (Halmes et al., 2000). Related data also are available from the stop studies with vinyl chloride (Drew et al., 1983). Analysis by Halmes et al. (2000) showed that, for six of the eleven chemicals and half the tumor sites, the assumption that the cancer risk would be equal when the product of concentration and time (i.e., C x T) was constant was incorrect, and usually underestimated risk, as more of the risk came from the beginning of the exposure rather than the end. This dependence of risk on both duration and intensity of exposure did not appear to be correlated with mutagenicity. It should be noted that these stop studies all involved exposures early in the life of the animal (as opposed to a limited number of cancer studies that looked at later periods of life; e.g., Drew et al., 1983), but the extent to which the differences in tumor outcome result from increased susceptibility in these early periods or the extended period for expression of the cancer cannot be evaluated. These stop studies also used doses as high as or higher than the highest dose used in the two-year exposure. This latter factor clearly had a significant effect for two chemicals, causing tumors at higher doses that were not observed at lower doses. These results suggest that pharmacokinetic or other dose-rate dependencies can make the effects of exposures at high doses different from those exposures at lower doses. While not directly informative about early childhood exposures, these studies provide a perspective on the common cancer risk assessment practice of averaging exposures over a lifetime, especially those that include earlier lifestages. Thus, alternative methods for estimating risks from short-term exposures during childhood should be considered.

Information on different lifestage susceptibilities to cancer risks for humans exists for ionizing radiation. The effects of chemical mutagens at different lifestages on cancer induction are derived from laboratory animal studies. While the induction of cancer by ionizing radiation and the induction of cancer by chemical mutagens are not identical processes, both involve direct damage to DNA as critical causal steps in the process. In both cases, the impacts of early exposure can be greater than the impacts of later exposures, probably due to some combination of early-lifestage susceptibility and the longer periods for observation of effects. As indicated in Tables 9 and 10, A-bomb survivors exhibited different lifestage dependencies at different tumor sites, though the total radiation-related incidence of tumors showed a general slow decline with age at exposure. However, as previously noted, there are apparent differences at some sites between the two tables. In addition to the sampling and modeling differences, the excess risk values in Table 9 are based on Japanese baselines while the coefficients in Table 10 reflect UNSCEAR's effort to transport the risks from the Japanese population to that of the United States. However, it is clear that the total radiation-related tumor incidence showed a general slow decline with age at exposure.

The studies in rodents of chemicals with mutagenic modes of action similarly support a

general decline in induced cancer risk with age at exposure and similarly show some differences for individual tumor sites. In general, the earliest two or three postnatal weeks in mice and rats appeared to be the most susceptible, though some degree of increased susceptibility through puberty in rats (beginning around 5–7 weeks) and mice (beginning around 4–6 weeks) for some types of tumors exists.

All the acute dosing studies that demonstrated carcinogenicity with animals of different ages used chemicals with a mutagenic mode of action (Tables 4 and 6). These studies provide the clearest demonstrations of periods of differential susceptibility because the exposure rate is constant at the different ages. The repeated dose studies also include several of the most informative studies for assessing perinatal carcinogenesis, notably those on vinyl chloride and DEN (Tables 2 and 4). The vinyl chloride studies by Maltoni and colleagues are part of a large series of studies on this compound that included exposures to different concentrations for varying durations, including some at early lifestages (Maltoni et al., 1984). The DEN study by Peto et al. (1984) used a unique chronic study design in which groups of rats were exposed to multiple drinking water concentrations starting at 3, 6, or 20 weeks of life. This design provides information on the susceptibility of early exposure periods within a nearly lifetime exposure.

Beyond the analysis described here, there are conceptual biological rationales that would suggest DNA-damaging agents would have greater impacts on early lifestages. Growth involves substantial levels of cell replication, even in organs that in adults are only very slowly replicating, thus increasing the likelihood that a cell will undergo division before the DNA damage caused by the mutagen has been repaired. Increased replication also can lead to a greater division of initiated cells, leading to a larger number of initiated cells per specified dose. These periods of cell replication can vary for different tissues. For example, DMBA appears to be more effective at initiating mammary tumors in 6-8 week old rats, which are undergoing development of that tissue, than during earlier or later periods (Meranze et al., 1969). While tumor promotion processes can be very dependent upon the duration of promotion, initiation processes can occur in relatively brief periods (e.g., the single-dose studies in animals or radiation exposure in humans). Most tumors take extended periods to develop, making damage that occurs earlier in life more likely to result in tumors prior to death than would exposures that occur later in life. While some of these observations may also pertain to other modes, all of them (with some differences among tumor sites) appear to be potentially relevant to a greater susceptibility to mutagenic modes of action during early-life stages (vs. later-life stages).

The information on lifestage susceptibility for chemicals inducing cancers through modes of action other than direct DNA interaction is more varied, showing an increase in tumor incidence during perinatal exposure versus exposures of mature animals (e.g., polybrominated

biphenyls induced liver tumors), no tumors from perinatal exposure (e.g., ethylene thiourea induced thyroid tumors), no effect of combined perinatal and adult exposure (e.g., DPH liver tumors in rats and female mice), and different tumors from perinatal exposure versus adult exposure (e.g., DES, ascorbate). These variations are likely a result of the modes of action of these chemicals and the pharmacokinetic differences in doses during different periods of life. No studies were evaluated that were directly comparable to the single-dose studies with mutagens, which clearly show significant differences in tumor responses after explicitly controlled doses at different lifestages.

Some evidence for an effect of early-lifestage exposures on tumor incidence was observed in studies with polybrominated biphenyls, amitrole, DDT, dieldrin, and diphenylhydantoin. These studies show increased incidence of tumors in mice from perinatal exposure, though only those for polybrominated biphenyls were statistically significant. (A nonstatistically significant increase also was observed in male rats with polybrominated biphenyls.) Combined perinatal and adult exposures generally gave statistically significant increases, though not necessarily for each sex and species (rat and mice) in the diphenylhydantoin and polybrominated biphenyl studies.

There are important demonstrations of chemicals acting through modes of action other than mutagenic to cause different tumor types with early-lifestage exposures compared with exposures for adults, e.g., tamoxifen and DES (Carthew et al., 2000; Carthew et al., 1996, Gass et al., 1964; Newbold et al., 1990, 1997, 1998). In addition, studies with *in utero* exposure to atrazine (Fenton and Davis, 2002), DES, and arsenic (Waalkes et al., 2003) indicate that early-life exposures to compounds can alter susceptibility of endocrine and reproductive organs. Three of these compounds (i.e., DES, genistein, and tamoxifen) bind to the estrogen receptor. Ongoing studies on ethinyl estradiol, nonylphenol, and genistein by the National Toxicology Program will add to this database for estrogens (Laurenzana et al., 2002; Newbold et al., 2001). These studies will evaluate cancer incidence in offspring exposed *in utero*, during lactation, and through adulthood via diet. A study with genistein found uterine tumor development to be dependent upon early-lifestage exposures (Newbold et al., 2001). Another recent study of estrogen found a shorter latency for mammary tumors in mice exposed at 8 and 12 weeks as compared to mice exposed at 4 or 18 weeks, indicating a susceptible period between 8 to 12 weeks of exposure (Yang, 2003). Thus, there is an actively growing database from which to consider issues of childhood exposure and cancer for compounds acting through the estrogen receptor or other mechanisms of endocrine disruption.

The ability to estimate with any accuracy the juvenile to adult cancer potency ratio depends very much on the experimental design used. The lifetime design has less ability to

distinguish increased susceptibility from early-life exposure than the other types of designs. Consider two different experimental designs. In the first, the "lifetime" design, a group of animals are exposed starting as juveniles, and exposure continues through adulthood. A second group are exposed only in adulthood, and the juvenile:adult ratio results from a comparison of tumor incidences in the two groups. In the second, the "repeated" design, one group of animals is exposed only during the juvenile period, and is then followed through adulthood to assess tumor incidence, and a second group of animals is exposed only through adulthood. The lifetime design turns out to be a particularly insensitive design for estimating the juvenile:adult ratio.

The following example demonstrates the magnitude of the problem: Suppose the risk per day of exposure of a chemical is ten fold greater in the juvenile period as in the adult period, and animals exposed through adulthood at a particular dose level have an extra risk of 60% for having at least one tumor, while 1% of control animals have tumors. The adult exposure period is 94 weeks, while the juvenile exposure period is 4 weeks. Thus, in the lifetime design, the group of animals exposed as juveniles will receive a total of 98 weeks of exposure, (4 in juvenile and 94 in adult), while those receiving the adult-only exposure receive 94 weeks of exposure. In the repeated design, animals exposed as juveniles receive only 4 weeks of exposure, while the adults receive 94 weeks, just as in the lifetime design. Each group starts with 50 animals. Under these assumptions, using equations (1) and (2) from Section 2.3, the expected number of animals with tumors in the three treatment groups (control, juvenile-exposed, adult-exposed groups) in the two designs is:

	Number of animals with tumors		
	Control	**Early-life exposure**	**Adult exposure**
Lifetime	1	36	30
Repeated	1	16	30

Notice that in the "lifetime" design, only six more juvenile-exposed animals have tumors than in the adult-exposed group, whereas in the "repeated" design, 16 juvenile-exposed animals have tumors. The data in the lifetime design are consistent with the hypothesis of no tumors being induced during the juvenile period: the ratios 36/50 and 30/50 are not statistically significantly different. In other words, the data from the lifetime design are statistically consistent with the hypothesis of *no risk at all* during the juvenile period, even though the real response is a 10 times greater risk from early-life exposure. The difference between the results from the two different study designs is due to the one-hit model: each additional week of a long exposure contributes less than the previous week to the total number of animals with tumors.

Note that, even if the one-hit model is not correct, chronic exposure probably results in a non-statistically significant increase for the lifetime exposure including juveniles as compared with only adult exposure.

The proper measure of relative potency of an exposure in the juvenile period relative to an exposure in the adult period is the ratio of doses in the two periods that give the same incidence of tumors. However, most of the data sets used in this report contained only one non-control dose, precluding the extensive dose-response modeling that would be required to estimate this ratio of doses. However, this document largely considered chemicals for which a mutagenic mode of action has been established and for which a linear, no-threshold dose-response function is assumed for the low-dose range being considered for risk assessment. In the case of the linear dose-response function, the analysis of the relative response from the same dose will produce the same value as ratio of doses that produces the same incidence of tumors.

For a one-hit dose-response equation, the probability of developing a tumor after the same dose and duration in the juvenile or adult period is

$$P_a = 1-(1-P_0)e^{-m_a x}$$
$$P_j = 1-(1-P_0)e^{-m_j x}$$

for dose x. Suppose we want to calculate the dose D_a or D_j that results in a given incidence of tumors after an adult or juvenile exposure. From equation 1, D_a and D_j equal:

$$D_a = \frac{-\ln\left(\frac{1-P_c}{1-P_0}\right)}{m_a}$$
$$D_j = \frac{-\ln\left(\frac{1-P_c}{1-P_0}\right)}{m_j}$$

Thus, the ratio $D_a/D_j = m_j/m_a$, the ratio calculated in this document.

In summary, this analysis supports the conclusion that there can be greater susceptibility for the development of tumors as a result of exposures to chemicals acting through a mutagenic mode of action, when the exposures occur in early lifestages as compared with later lifestages. Thus, this Supplemental Guidance recommends for chemicals with a mutagenic mode of action for carcinogenesis when chemical-specific data on early-life exposure are absent, a default

approach using estimates from chronic studies (i.e., cancer slope factors) with appropriate modifications to address the potential for differential risk of early-lifestage exposure. For chemicals acting through a non-mutagenic mode of action, e.g., hormonally mediated carcinogens, the available data suggest that other approaches may need to be developed for addressing cancer risk estimates from childhood exposures. This is a particular concern because the tumors arising from hormonally active chemicals appear to involve different sites when exposure is during early-life versus adulthood, an effect that has been observed relatively infrequently. Development of such approaches would require additional research to provide an expanded scientific basis for their support, including additional research and the possible development of new toxicity testing protocols that consider early lifestage dosing.

The current data do also not allow analysis of some issues of potential interest for risk assessment, e.g., potential increased risk of childhood cancer, from *in utero* or childhood exposures. Assessing the role of environmental exposures on childhood cancers is difficult, but additional research could include epidemiological studies or experimental studies with animals genetically designed to express cancers analogous to human childhood cancers. Rigorous quantification of exposure doses at different lifestages and in rodent pups in experimental studies would be useful for evaluating whether there is greater childhood susceptibility. Pharmacokinetic modeling could better define the internal doses to improve determination of the magnitude of increased susceptibility.

5. GUIDANCE FOR ASSESSING CANCER RISKS FROM EARLY-LIFE EXPOSURE

Consistent with the approach and recommendations of the U.S. EPA cancer risk assessment guidelines (U.S. EPA, 2004), any assessment of cancer susceptibility will begin with a critical analysis of the available information. Figure 3 shows the proposed steps in the process. The potential for increased susceptibility to cancer from early-life exposure, relative to comparable exposure later in life, generally warrants explicit consideration for each assessment.

When developing quantitative estimates of cancer risk, the Agency recommends integration of age-specific values for both exposure and toxicity/potency where such data are available and appropriate. Children, in general, are expected to have some exposures that differ from those of adults (either higher or lower), due to differences in size, physiology, and behavior. For example, children are generally assumed to eat more food and drink more water relative to their body weight than adults. Children's normal activities, such as putting their hands into their mouths or playing on the ground, can result in exposures to contaminants that adults do not encounter. Moreover, children and adults exposed to the same concentration of an agent in food, water, or air may receive different (higher or lower) internal doses due to differences, for example, in intake, metabolism, or absorption rates. Children are less likely than adults to be exposed to products typically used in industrial settings and often have more limited diets than adults. When assessing risks, if the data are available and relevant, it is important to include exposure that is measured or modeled for all lifestages, including exposures during childhood and during adulthood. EPA continues to develop better tools for assessing childhood exposure differences, such as the *Child-Specific Exposure Factors Handbook* (U.S. EPA, 2002a), and models, such as Stochastic Human Exposure and Dose Simulation (SHEDS) and Consolidated Human Activity Database (CHAD) (McCurdy et al., 2000; Zartarian et al., 2000)

Mode-of-action studies can be a source of data on quantitative differences between children and adults (Figure 3, Box 1). If the available information is sufficient to establish the agent's mode of action for early-life and adult exposures, then the implications for early-life exposure of that mode of action are used to develop separate risk estimates for childhood exposure. Pertinent information can be obtained both from agent-specific studies and from other

studies that investigate the general properties of the particular mode of action. All data indicating quantitative differences between children and adults are considered in developing those portion(s) of the risk estimates for exposure estimates that include childhood exposure. Some examples include the potential for children to have a different internal dose of the active agent or a change in a key precursor event (see Section 2.4.3.4 of the *Guidelines for Cancer Risk Assessment*).

When the mode of action cannot be established (Figure 3, Box 2), the policy choice would be to use linear extrapolation to lower doses such that risk estimates are based on a lifetime average daily exposure without further adjustment. No general adjustment is recommended at this time. This policy choice is consistent with past U.S. EPA practice that has been favorably evaluated over the years. The result would be expected to produce plausible upper bound risk estimates, based on the use of linear extrapolation as a default in the absence of information on the likely shape of the dose-response curve.

When a mode of action other than mutagenicity is established, if it is nonlinear (Figure 3, Box 3) or linear (Figure 3, Box 4), no general adjustment is recommended at this time. Although the available studies (discussed previously) indicates that higher or lower cancer risks may result from early-life exposure, there is insufficient information or analyses currently available to determine a general adjustment at this time. As other modes of action become better understood, this information may include data on quantitative differences between children and adults. If such data are available, an analysis of the differences could be used to adjust risk estimates for childhood exposure. EPA expects to expand this Supplemental Guidance to specifically address modes of action other than mutagenicity when sufficient data are available and analyzed.

When the data indicate a mutagenic mode of action,[5] the available studies (discussed

5 Determination of chemicals that are operating by a mutagenic mode of action entails evaluation of test results for genetic endpoints, metabolic profiles, physicochemical properties, and structure-activity analyses in a weight-of-evidence approach (Waters et al., 1999). Established protocols are used to generate the data (Cimino, 2001; OECD, 1998; U.S. EPA, 2002b); however, it is recognized that newer methods and technologies such as those arising from genomics can provide useful data and insights to a mutagenic mode of action. Carcinogens acting through a mutagenic mode of action generally interact with DNA and can produce such effects as DNA adducts and/or breakage. Carcinogens with a mutagenic mode of action often produce positive effects in multiple test systems for different genetic endpoints, particularly gene mutations and structural chromosome aberrations, and in tests performed *in vivo*, which generally are supported by those performed *in vitro*. This mode of action is addressed in more detail in Section 2.3.5 of EPA's cancer guidelines (U.S. EPA, 2005).

above) indicate higher cancer risks resulting from a given exposure occurring early in life when compared with the same amount of exposure during adulthood. However, chemical-specific data relating to mode of action (e.g., toxicokinetic or toxicodynamic information) may suggest that even though a compound has a mutagenic mode of action, higher cancer risks may not result. Such data should be considered before applying the age-dependent adjustment factors.

If the available, chemical-specific information includes an epidemiologic study of the effects of childhood exposure or an animal bioassay involving early-life exposure (Figure 3, Box 5), then these studies are analyzed to develop risk estimates (i.e., cancer slope factors) that specifically address any potential for differential potency in early lifestages. An example is the IRIS assessment of vinyl chloride (U.S. EPA, 2000b; c).

In the absence of early-life studies on a specific chemical under consideration (Figure 3, Box 6), the extrapolation from the point of departure to lower doses employs linear extrapolation (see Section 3.3.1 of the U.S. EPA [2005] cancer guidelines). This choice is based on mode-of-action data indicating that mutagens can give rise to cancers with an apparently low-dose linear response. Adjustments to the resultant risk estimates are specified with regard to childhood exposures. This approach is adopted because risk estimates based on an average daily exposure prorated over a lifetime do not consider the potential for higher cancer risks from early-life exposure.

The adjustments described below reflect the potential for early-life exposure to make a greater contribution to cancers appearing later in life. The 10-fold adjustment represents an approximation of the weighted geometric mean tumor incidence ratio from juvenile or adult exposures in the repeated dosing studies (see Table 8). This adjustment is applied for the first 2 years of life, when toxicokinetic and toxicodynamic differences between children and adults are greatest (Ginsberg et al., 2002; Renwick, 1998). Toxicokinetic differences from adults, which are greatest at birth, resolve by approximately 6 months to 1 year, while higher growth rates extend for longer periods. The 3-fold adjustment represents an intermediate level of adjustment that is applied after 2 years of age through <16 years of age. This upper age limit represents middle adolescence following the period of rapid developmental changes in puberty and the conclusion of growth in body height in NHANES data (Hattis et al., 2005). Efforts to map the approximate start of mouse and rat bioassays (i.e., 60 days) to equivalent ages in humans ranged from 10.6 to 15.1 years (Hattis et al., 2005). Data are not available to calculate a specific dose-response adjustment factor for the 2 to <16-year age range, so EPA selected the 3-fold

adjustment because it reflects a midpoint, i.e., approximately half the difference between 1 and 10 on a logarithmic scale ($10^{1/2}$), between the 10-fold adjustment for the first two years of life and no adjustment (i.e., 1-fold) for adult exposure. EPA also recognizes that exposures occurring near the end of life may have little effect on lifetime cancer risk, but lacks adequate data at present to provide an adjustment for this "wasted dose" effect. Similarly, since most of the studies involved only one latency period, the potential effect of early-life exposure on latency for the observed tumors could not be evaluated. The lack of data on effect on latency also limited the types of analyses that could be performed, e.g., more complex dose-response functions, such as multi-stage or clonal expansion models, could not be evaluated. Thus, the potential effects of early-life exposures on latency were not evaluated. Finally, as the adjustment factors are derived from a weighted geometric mean of the data evaluated, these adjustment will both over-estimate and under-estimate the potential potency for early-life exposure for chemicals with a mutagenic mode of action for carcinogenesis. An examination of the data in the tables demonstrates that some of the ratios were less than one, while others exceeded 10. For this reason, the Supplemental Guidance emphasizes that chemical-specific data should be used in preference to these default adjustment factors whenever such data are available.

The following adjustments represent a practical approach that reflects the results of the preceding analysis, which concluded that cancer risks generally are higher from early-life exposure than from similar exposure durations later in life:

- For exposures before 2 years of age (i.e., spanning a 2-year time interval from the first day of birth up until a child's second birthday), a 10-fold adjustment.

- For exposures between 2 and <16 years of age (i.e., spanning a 14-year time interval from a child's second birthday up until their sixteenth birthday), a 3-fold adjustment.

- For exposures after turning 16 years of age, no adjustment.

Clearly other age groups, such as an age group experiencing pubertal changes in physiology, or approximately ages 9 - 15, may experience changes in biological processes that could lead to modifications in the susceptibility to the effects of some carcinogens, depending on the mode of action. This Supplemental Guidance focuses on carcinogens with a mutagenic mode

of action. For any mode of action, the Agency is interested in identifying lifestages that may be particularly sensitive or refractory for carcinogenesis, and believes that the mode of action framework as described by EPA's cancer guidelines (U.S. EPA, 2005), is an appropriate mechanism for elucidating these lifestages. In general, the Agency's analyses of lifestages that may be susceptible will depend on three factors: (1) establishing the mode of action for carcinogenesis; (2) using knowledge about the biological and toxicological key events in that mode of action that are likely to be affected by lifestages; and (3) the availability, or development, of data that allow analysis of the effects of chemicals acting by that mode of action during the relevant ages. For each mode of action evaluated, therefore, the various age groupings determined to be at a differential risk, which may differ significantly from those proposed for the mutagenic mode of action, are expected to be evaluated independently of other modes of action. When data, including well established mode of action data, are available that allow specific evaluation of lifestage differences in toxicokinetics or toxicodynamics that would lead to lesser or greater susceptibility from early-life exposures to carcinogens, then those data should be used, as generally discussed in EPA's cancer guidelines (U.S. EPA, 2005), in preference to the default procedures described in this Supplemental Guidance.

The 10-fold and 3-fold adjustments in slope factor are to be combined with age-specific exposure estimates when estimating cancer risks from early life exposure to carcinogens that act through a mutagenic mode of action. It is important to emphasize that these adjustments are combined with corresponding age-specific estimates of exposure to assess cancer risk. For example, for a 70-year lifetime, where there are data showing negligible exposure to children, the estimated cancer risk from childhood exposure would be also negligible and the lifetime cancer risk would be reduced to that resulting from the relevant number of years of adult exposure (in the absence of specific information, 55 years). Where there are data (measured or modeled) for childhood exposures, the age-group specific exposure values are used along with the corresponding adjustments to the slope factor. Where there are no relevant data or models for childhood exposures and only lifetime average exposure data are available, the lifetime exposure data are used with the adjustments to the slope factor for each age segment.

It is recognized that, when the exposure is fairly uniform over a lifetime, the effect of these adjustments on estimated lifetime cancer risk are small relative to the overall uncertainty of

such estimates. These adjustments can be applied when estimating the cancer risk resulting from childhood exposure. These adjustments are applied when developing risk estimates from conventional animal bioassays or epidemiologic studies of effects of adult exposure. Some examples follow in the next section.

The Agency has also carefully considered both the advantages and disadvantages to extending the default potency adjustment factors to carcinogenic chemicals for which the mode of action remains unknown. It is the Agency's long-standing science policy position that use of the linear low-dose extrapolation approach (without further adjustment) provides adequate public health conservatism in the absence of chemical-specific data indicating differential early-life susceptibility. At the present time, therefore, EPA is recommending these age-dependent adjustment factors only for carcinogens acting through a mutagenic mode of action based on a combination of analysis of available data and the above-mentioned science policy position. In general, the Agency prefers to rely on analyses of data, rather than general defaults. When data are available for a susceptible lifestage, they should be used directly to evaluate risks for that chemical and that lifestage on a case-by-case basis. In this analysis, the data for non-mutagenic carcinogens, when the mode of action is unknown, were judged to be too limited and the modes of action too diverse to use this as a category for which a general default adjustment factor approach can be applied.

6 COMBINING LIFESTAGE DIFFERENCES IN EXPOSURE AND DOSE-RESPONSE WHEN ASSESSING CARCINOGEN RISK - SOME EXAMPLES FOR CARCINOGENS THAT ACT THROUGH A MUTAGENIC MODE OF ACTION

It is important for the risk assessor to consider lifestage differences in both exposure and dose-response when assessing cancer risk resulting from early-life exposures. As discussed in Section 5, age dependent adjustments factors (ADAFs) in dose response (i.e., slope factors) are combined with age specific exposure estimates when assessing cancer risks. This is a departure from the way cancer risks have historically been based upon the premise that risk is proportional to the daily average of lifetime dose. This Supplemental Guidance recommends an integrative approach that can be used to assess total lifetime risk resulting from lifetime or less-than-lifetime exposure during a specific portion of a lifetime.

The following examples can help demonstrate how to apply this guidance by integrating potential lifestage differences in exposure and/or dose-response (potency), and also demonstrate what the resulting impacts are on calculated risks. These hypothetical examples consider risks from both lifetime, as well as less-than-lifetime oral exposures. Risks associated with inhalation exposure to carcinogens that act via a mutagenic mode of action are calculated in similar fashion by applying the appropriate ADAF(s) along with the corresponding inhalation unit risk estimate, using pertinent estimates of exposure concentration.

Note again, ADAFs are only to be used for agents with a mutagenic mode of action for carcinogenesis when chemical-specific data are absent. For all modes of action, when chemical-specific data are available for early-life exposure, those data should be used.

6.1 CALCULATING LIFETIME RISKS ASSOCIATED WITH LIFETIME EXPOSURES

Example 1: Consider a scenario of exposure to a carcinogen with a **nonmutagenic** mode of action. Suppose the oral cancer slope factor derived from a typical animal study (i.e., where dosing begins after puberty) is estimated to be 2 per mg/kg-d, and the exposure rate remains constant throughout life at 0.0001 mg/kg-d (this is equivalent to saying the daily average of lifetime dose rate is equal to 0.0001 mg/kg-d). The risk from lifetime exposure is calculated by multiplying the slope factor and the exposure rate:

$$\text{Risk} = (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d})$$

$= \quad 2 \times 10^{-4}$

<u>Example 2</u>: Now consider the same exposure scenario for a carcinogen with a **mutagenic** mode of action for which the oral cancer slope factor, derived from a typical animal study where dosing begins after puberty, is also estimated to be 2 per mg/kg-d. In this case, ADAFs are used, as follows.

a. To calculate lifetime risk for a population with average life expectancy of 70 years, sum the risk associated with each of the three relevant time periods:

- Risk during the first 2 years of life (where the ADAF = 10);
- Risk for ages 2 through < 16 (ADAF = 3); and
- Risk for ages 16 until 70 years (ADAF = 1).

Thus, risk equals the sum of:

- Risk for birth through < 2 yr = (2 per mg/kg-d) x 10 (ADAF) x (0.0001 mg/kg-d) x 2yr/70yr
  $= 0.6 \times 10^{-4}$
- Risk for ages 2 through < 16 = (2 per mg/kg-d) x 3 (ADAF) x (0.0001 mg/kg-d) x (13yr/70yr)
  $= 1.1 \times 10^{-4}$
- Risk for ages 16 until 70 = (2 per mg/kg-d) x 1 (ADAF) x (0.0001 mg/kg-d) x (55yr/70yr)
  $= 1.6 \times 10^{-4}$

Risk $= 0.6 \times 10^{-4} + 1.1 \times 10^{-4} + 1.6 \times 10^{-4}$

$= 3.3 \times 10^{-4}$

b. If exposure varies with age, then such differences are also included. Now suppose the same example as immediately above, except that exposure for ages 1 through <12 was twice as high as exposure for all other ages. In this case, sum the risk associated with each of the five relevant time periods in which exposure rates and/or potencies (slope

factors) vary:

Risk equals the sum of:

- Risk for birth through < 1 yr (1yr) = (2 per mg/kg-d) x 10 (ADAF) x 0.0001 mg/kg-d x 1yr/70yr
  $= 0.3 \times 10^{-4}$
- Risk for ages 1 through < 2 (1yr) = (2 per mg/kg-d) x 10 (ADAF) x 0.0002 mg/kg-d x 1yr/70 yr
  $= 0.6 \times 10^{-4}$
- Risk for ages 2 through < 12 (10yr) = (2 per mg/kg-d) x 3 (ADAF) x 0.0002 mg/kg-d x 10yr/70yr
  $= 1.7 \times 10^{-4}$
- Risk for ages 12 through < 16 (4yr) = (2 per mg/kg-d) x 3 (ADAF) x 0.0001 mg/kg-d x 4yr/70yr
  $= 0.3 \times 10^{-4}$
- Risk for ages 16 until 70 years (55yr) = (2 per mg/kg-d) x 1 (ADAF) x 0.0001 mg/kg-d x 55yr/70yr
  $= 1.6 \times 10^{-4}$

Risk $= 0.3 \times 10^{-4} + 0.6 \times 10^{-4} + 1.7 \times 10^{-4} + 0.3 \times 10^{-4} + 1.6 \times 10^{-4}$
$= 4.5 \times 10^{-4}$

6.2 CALCULATING LIFETIME RISKS ASSOCIATED WITH LESS THAN LIFETIME EXPOSURES

If exposure only occurs for a limited number of years (for example, consider a family that lives near a source of exposure for a five-year period of time before moving away), it is critical to combine lifestage differences in exposure and dose-response for the relevant time interval. The examples presented below demonstrate how adjusting potency and/or exposure can affect the assessment of cancer risk.

Example 3: If exposure to a carcinogen with a mutagenic mode of action with an oral slope factor equal to 2 per mg/kg-d occurs during adulthood for only 5 years, the daily average of lifetime dose is time weighted to apportion risk for the number of years of exposure by a factor of 5/70:

$$\text{Risk} = (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d}) \times (5\text{yr}/70\text{yr})$$
$$= 1.4 \times 10^{-5}$$

Example 4: If this 5-year exposure occurs during childhood, the risk calculations are adjusted to consider the potential for higher potency from early-life exposure. Assessors should remember that the age dependent adjustment factors for carcinogens with a mutagenic mode of action are applied only to exposure periods occurring up to age 16.

a. For a child exposed between ages 5 and 10, only a 3-fold ADAF is applied because the exposure occurs entirely between ages 2 and <16 years:

$$\text{Risk} = 3 \text{ (ADAF)} \times (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d}) \times (5 \text{ yr}/70 \text{ yr})$$
$$= 4.3 \times 10^{-5}$$

b. For an exposure between ages 13 and <18, a 3-fold ADAF is applied only to the 3-year portion occurring before age 16:

Risk equals the sum of:

- Risk for ages 13 through < 16 (3yr) $= 3 \text{ (ADAF)} \times (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d}) \times (3 \text{ yr}/70 \text{ yr})$
  $= 2.6 \times 10^{-5}$
- Risk for ages 16 through < 18 (2yr) $= 1 \text{ (ADAF)} \times (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d}) \times (2 \text{ yr}/70 \text{ yr})$
  $= 0.6 \times 10^{-5}$

$$\text{Risk} = 2.6 \times 10^{-5} + 0.6 \times 10^{-5}$$

$= 3.2 \times 10^{-5}$

c. For a child exposed from birth through age 5, different ADAFs are applied to the periods before and after age 2:

Risk equals the sum of:

- Risk for birth through < 2 (2yr) $= 10$ (ADAF) x (2 per mg/kg-d) x (0.0001 mg/kg-d) x (2 yr/70 yr)
  $= 5.7 \times 10^{-5}$
- Risk for ages 2 through < 5 (3yr) $= 3$ (ADAF) x (2 per mg/kg-d) x (0.0001 mg/kg-d) x (3 yr/70 yr)
  $= 2.6 \times 10^{-5}$

Risk $= 5.7 \times 10^{-5} + 2.6 \times 10^{-5}$
$= 8.3 \times 10^{-5}$

Example 5: Lifetime risk calculations based on less-than-lifetime exposure to a carcinogen with a mutagenic mode of action include any lifestage changes in potency as well as exposure. In this example, again consider a scenario of 5 years of exposure to a carcinogen with a mutagenic mode of action, but suppose that the exposure rate is found to vary from 0.0002 mg/kg-d during the first 2 years of life, to 0.0001 mg/kg-d during the last 3 years.

a. For a child exposed between birth and age 5, sum the risk associated with the two relevant time periods:

Risk equals the sum of:

- Risk for birth through < 2 (2yr) = 10 (ADAF) x (2 per mg/kg-d) x (0.0002 mg/kg-d) x (2 yr/70 yr)
  $= 11.4 \times 10^{-5}$
- Risk for ages 2 through < 5 (3yr) = 3 (ADAF) x (2 per mg/kg-d) x (0.0001 mg/kg-d) x (3 yr/70 yr)
  $= 2.6 \times 10^{-5}$

Risk $= 11.4 \times 10^{-5} + 2.6 \times 10^{-5}$

$= 1.4 \times 10^{-4}$

b. For comparison, a similar risk calculation for 5 years of exposure later in life (after age 16) in which the first 2 years of exposure are double that of the next 3 years are carried out without any adjustment for potency:

Risk equals the sum of:

- Risk for first 2 years of adult exposure = 1 (ADAF) x (2 per mg/kg-d) x (0.0002 mg/kg-d) x (2yr/70yr)
  $= 1.1 \times 10^{-5}$
- Risk for final 3 years of adult exposure = 1 (ADAF) x (2 per mg/kg-d) x (0.0001 mg/kg-d) x (3yr/70yr)
  $= 0.9 \times 10^{-5}$

Risk $= 1.1 \times 10^{-5} + 0.9 \times 10^{-5}$

$= 2 \times 10^{-5}$

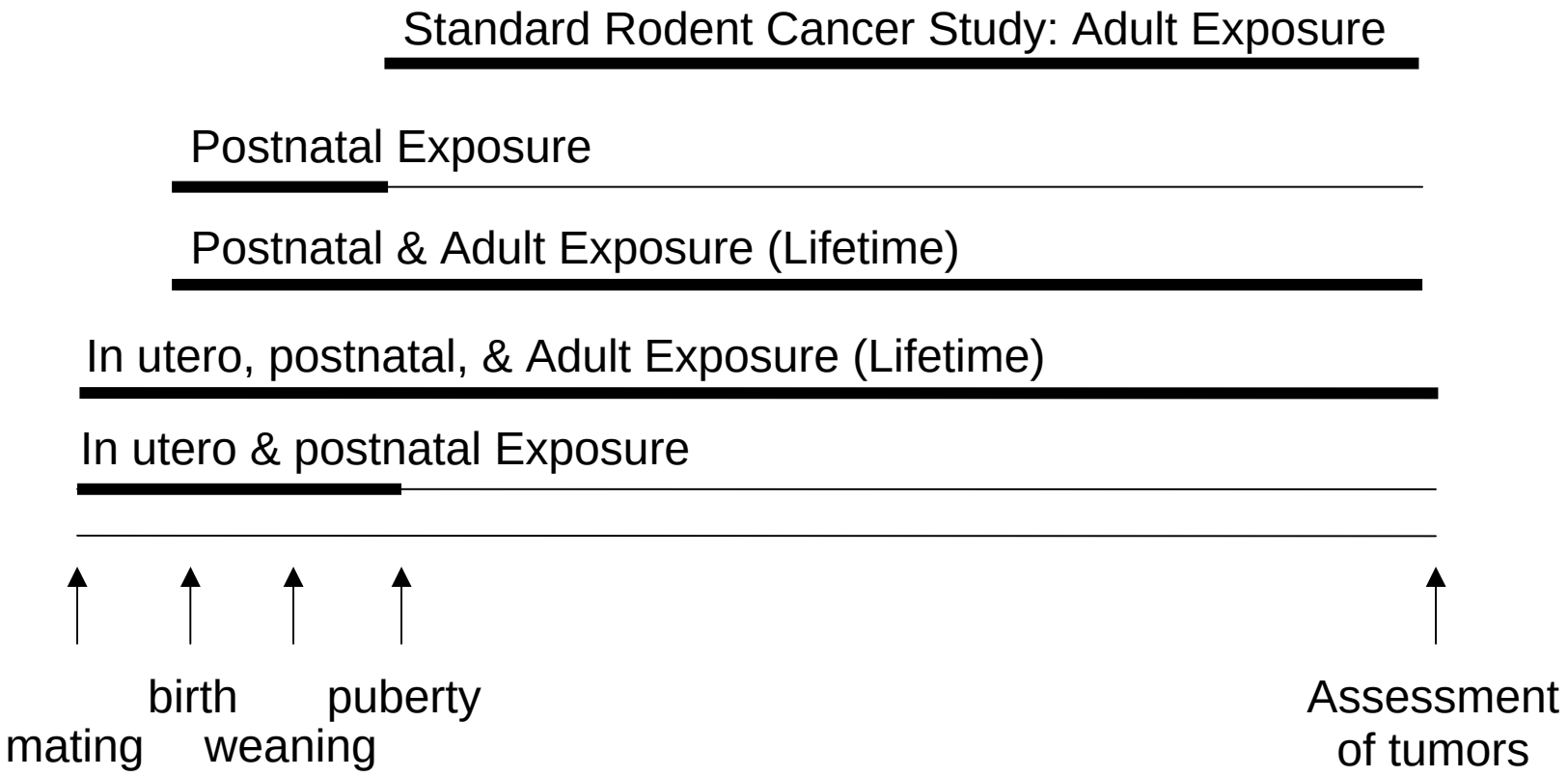

Figure 1. Study designs.

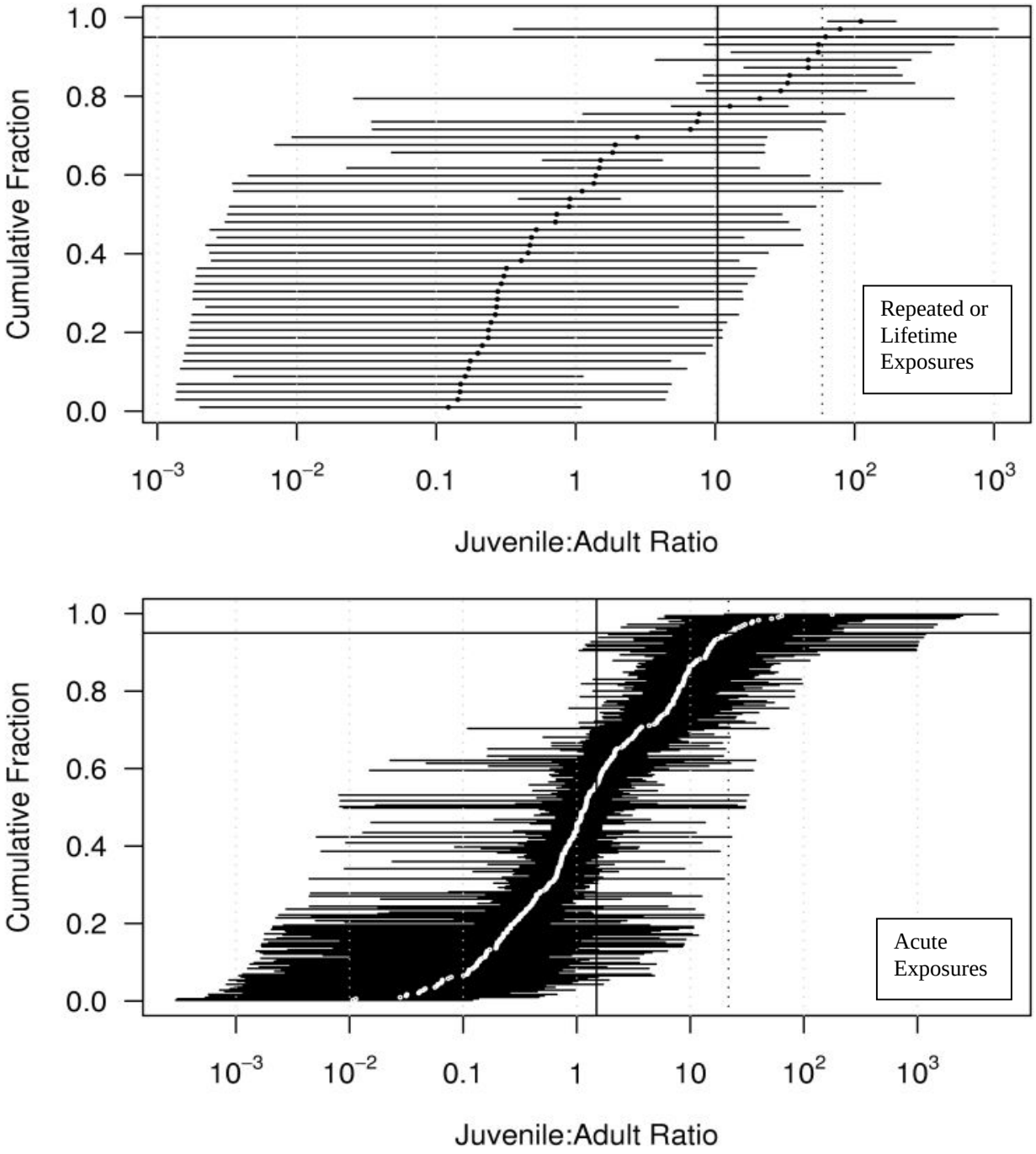

Figure 2: Posterior, unweighted geometric means and 95% confidence intervals for the ratios of juvenile to adult cancer potency for carcinogens acting primarily through a mutagenic mode of action. The top panel is for repeated and lifetime exposure studies (geometric mean in black), the bottom panel is for acute exposure studies mutagens (geometric mean in white). The horizontal lines to the left and right of each geometric mean correspond to 95% confidence limits. The vertical dark line represents the inverse-variance weighted geometric mean of the posterior geometric means. The horizontal dark line represents the 95th percentile of the unweighted distribution, with the vertical, dotted line establishing it value.

Figure 3. Flow chart for early-life risk assessment using mode of action framework

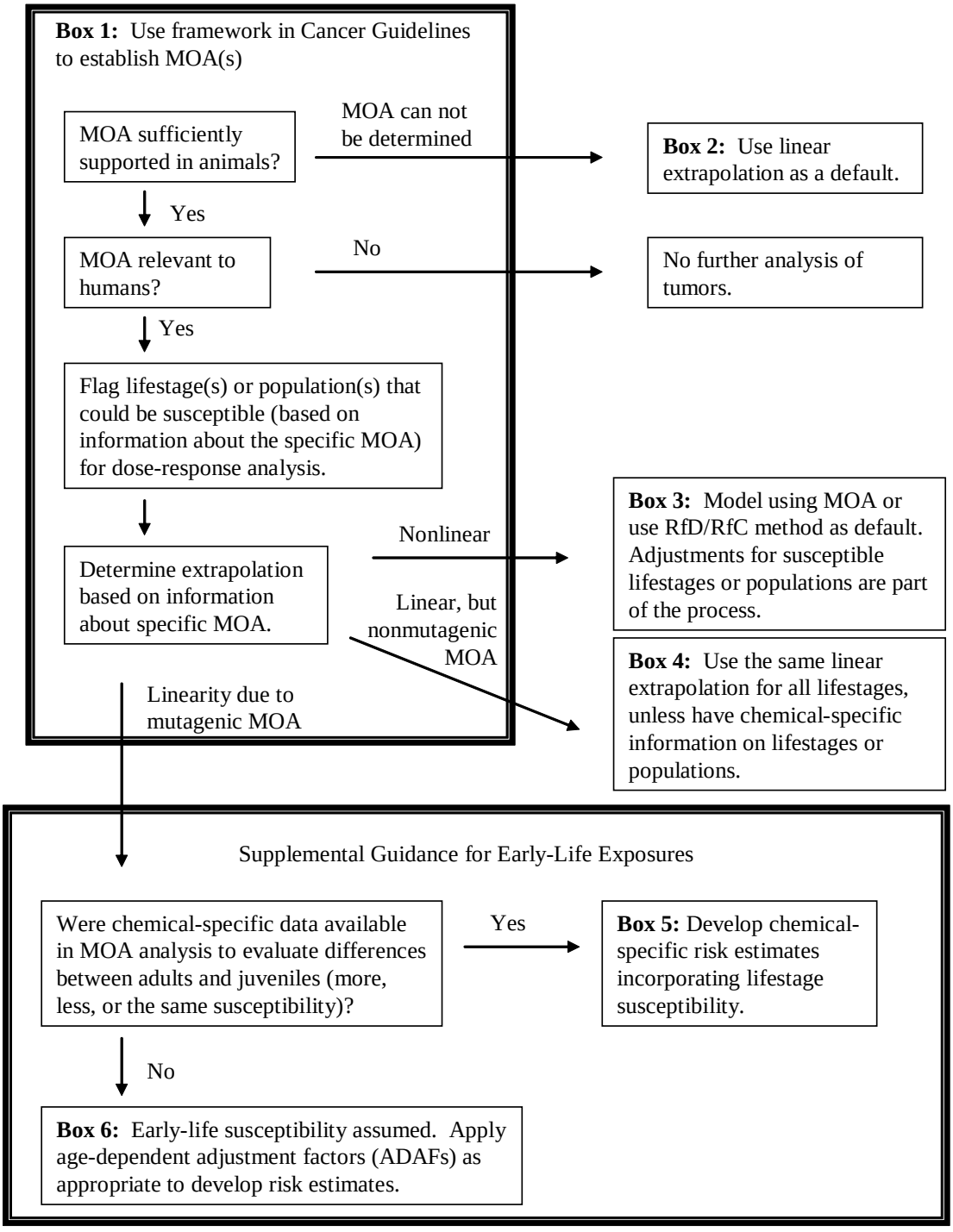

Table 1a. Chemicals that have been found to have carcinogenic effects from prenatal or postnatal exposure in animals as identified in different review articles

Chemical name	Review articles including prenatal and postnatal exposure					Chemicals selected for quantitative analysis
	Fujii (1991)	McClain et al. (2001)	Anderson et al. (2000)	Della Porta and Terracini (1969)	Other literature	
4-Acetylaminobiphenyl (AAB)	X					
4-Aminoazobenzene (AB)	X					
3-Amino-1,4,-dimethyl-5H-pyrido[4,3-b]indole (Trp-P-1)	X					
2-Aminodipyridol[1,2-a:3',2'-d]imidazole (Glu-P-2)	X					
2-Amino-6-methyldipyridol[1,2-a:3',2'-d]imidazole (Glu-P-1)	X					
3-Amino-1-methyl-5H-pyrido[4,3-b]indole (Trp-P-2)	X					
Amitrole						X
Arsenic					X	
5-Azacytidine			X			
3'-Azido-3'-deoxythymidine (AZT)			X			
Azoxymethane			X			
Benz[*a*]anthracene				X		
Benzidine			X			X
Benzo[*a*]pyrene (BaP)	X			X		X
1-(4'Bromophenylazo)-1-phenyl-1-hydroperoxymethane (BPH)	X					
N-Butyl-N-(3-carboxypropyl)nitrosamine (BCPN)	X					
N-Butyl-N-(3 hydroxbutyl)nitrosamine (BBN)	X					
Butylnitrosourea (BNU)	X					
Cyclophosphamide		X				
Dibenz[*a,h*]anthracene (DBA)				X		X
Dibutylnitrosamine (DBN)	X					
Dichlorodiphenyltrichloroethane (DDT)						X
Dieldrin						X
2-Diethylaminoethyl-2,2-dephenylvalerate hydrochloride (SKF 525A)	X					

Table 1a. Chemicals that have been found to have carcinogenic effects from prenatal or postnatal exposure in animals as identified in different review articles (continued)

Chemical name	Review articles including prenatal and postnatal exposure					Chemicals selected for quantitative analysis
	Fujii (1991)	McClain et al. (2001)	Anderson et al. (2000)	Della Porta and Terracini (1969)	Other literature	
Diethylnitrosamine (DEN)	X		X			X
Diethylstilbesterol (DES)			X			
4-Dimethylaminoazobenzene				X		
1,2-Dimethylhydrazine (DMH)	X					
7,12-Dimethylbenz[*a*]anthracene (DMBA)	X		X	X		X
Dimethylnitrosamine (DMN)	X		X	X		X
5',5'-Diphenylhydantoin (DPH)						X
Estradiol	X	X				
6-Ethoxy-2,2,4-trimethyl-1,2-dihydroquinoline (Santoquin)	X					
Ethylene thiourea (ETU)						X
Ethyl methane sulphonate				X		
Ethylnitrosobiuret			X			
Ethylnitrosourea (ENU)			X			X
N-2-Fluorenylacetamide (FAA)	X			X		
Genistein					X	
3-Hydroxyl-4-acetylaminobiphenyl (N-OH-AAB)	X					
N-2-Hydroxy-N-2-fluorenylacetamide (N-OH-FAA)	X					
2-Hydroxypropyl-propylnitrosamine			X			
9-Methylanthracene				X		
Methyl-2-benzylhydrazine			X			
Methylcholanthrene			X	X		
3-Methyl-4-dimethylaminoabenzene (3'ME-DAB)	X					
4-(Methylnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK)			X			
Methylnitrosourea (NMU)			X			
Methylnitrosourethane			X			
1-Methyl-3-nitro-1-nitrosoguanidine (MNNG)	X					

Table 1a. Chemicals that have been found to have carcinogenic effects from prenatal or postnatal exposure in animals as identified in different review articles (continued)

Chemical name	Review articles including prenatal and postnatal exposure					Chemicals selected for quantitative analysis
	Fujii (1991)	McClain et al. (2001)	Anderson et al. (2000)	Della Porta and Terracini (1969)	Other literature	
2-Naphthylamine				X		
2-Naphthylhydroxyamine				X		
Nickel acetate			X			
N-Nitrosobuylamine			X			
4-Nitroquinoline-1-oxide			X	X		
N-Nitrosomethyl(2-oxopropyl)amine			X			
2-Oxopropyl-propylnitrosamine			X			
1-Phenyl-3,3',-dimethylhydrzine			X			
1-Phenyl-3,3,-dimethyltriazene			X			
Polybrominated biphenyls (PBBs)						X
Safrole (3,4-methylenedioxyally benzene)	X		X			X
Soot	X					
Sterigmatocystin	X					
Tamoxifen					X	
1,3,5-Trimethyl-2,4,6-tris[3,5-di-tert-butyl-4-hydroxybenzyl]benzene (Ionox 33)	X					
Urethane (ethyl carbamate)			X	X		X
Vinyl chloride						X

Table 1b. List of chemicals considered in this analysis. (These are chemicals for which both early-life and adult exposure are reported in the same animal experiment.)

Chemical	References	Study type	Mutagenic mode of action
Amitrole	Vesselinovitch (1983)	Repeat dosing	
Benzidine	Vesselinovitch et al. (1975b)	Repeat dosing	X
Benzo[*a*]pyrene (BaP)	Vesselinovitch et al. (1975a)	Acute exposure	X
Dibenzanthracene (DBA)	Law (1940)	Acute exposure	X
Dichlorodiphenyltrichloroethane (DDT)	Vesselinovitch et al. (1979)	Repeat dosing Lifetime exposure	
Dieldrin	Vesselinovitch et al. (1979)	Repeat dosing Lifetime exposure	
Diethylnitrosamine (DEN)	Peto et al. (1984)	Lifetime exposure	X
	Vesselinovitch et al. (1984)	Acute exposure	
Dimethylbenz[*a*]anthracene (DMBA)	Meranze et al. (1969)	Acute exposure	X
	Pietra et al. (1961)	Acute exposure	
	Walters (1966)	Acute exposure	
Dimethylnitrosamine (DMN)	Hard (1979)	Acute exposure	X
Diphenylhydantoin, 5,5- (DPH)	Chhabra et al. (1993b)	Repeat dosing Lifetime exposure	
Ethylnitrosourea (ENU)	Naito et al. (1981)	Acute exposure	X
	Vesselinovitch et al. (1974)	Acute exposure	
	Vesselinovitch (1983)	Acute exposure	
Ethylene thiourea (ETU)	Chhabra et al. (1992)	Repeat dosing Lifetime exposure	
3-Methylcholanthrene (3-MU)[a]	Klein (1959)	Repeat dosing	X
Methylnitrosourea (NMU)	Terracini and Testa (1970) Terracini et al. (1976)	Acute exposure Acute exposure	X
Polybrominated biphenyls (PBBs)	Chhabra et al. (1993a)	Repeat dosing Lifetime exposure	
Safrole	Vesselinovitch et al. (1979)	Repeat dosing Lifetime exposure	X
Urethane	Chieco-Bianchi et al. (1963) Choudari Kommineni et al. (1970) De Benedictis et al. (1962) Fiore-Donati et al. (1962)	Acute exposure Acute exposure Acute exposure Acute exposure	X
	Klein (1966)	Acute exposure Lifetime exposure	
	Liebelt et al. (1964)	Acute exposure	
	Rogers (1951)	Acute exposure	
Vinyl chloride (VC)	Maltoni et al. (1984)	Repeat dosing	X

[a] Formerly known as 20-methylcholanthrene.

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Amitrole	Mice ($B6C3F_1$)	liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/98 (1%)	0/96 (0%)	Incidences are mice with adenomas or carcinomas.	Vesselinovitch (1983)
			Gestation day 12	Diet, to mothers	500 ppm	Gestation day 12 to delivery		6/74 (8%)[b]	0/83 (0%)[b]		
			Newborn	Diet, to mothers	500 ppm	Birth until weaning		10/45 (22%)[b]	0/55 (0%)[b]		
			At weaning	Diet, to offspring	500 ppm	From weaning to 90 weeks		20/55 (36%)[b]	9/49 (18%)[b]		
Benzidine	Mice ($B6C3F_1$)	liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/98 (1%)	0/100 (0%)	Higher sensitivity in males during perinatal period, in females during adulthood. Incidences are mice with adenomas or carcinomas.	Vesselinovitch et al. (1975b) Vesselinovitch et al. (1979a)
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 to delivery		17/55 (31%)[c]	2/62 (3%)[d]		
			Newborn	Diet, to mothers	150 ppm	Birth until weaning		62/65 (95%)[c]	2/43 (5%)[d]		
			At weaning	Diet, to offspring	150 ppm	From weaning to 90 weeks		22/50 (44%)[c]	47/50 (94%)[c]		
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 until weaning		49/49 (100%)[c]	12/48 (25%)[c]		
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 until 90 weeks		50/50 (100%)[c]	47/50 (94%)[c]		
DDT Dichlorodiphenyl-trichloroethane	Mice ($B6C3F_1$)	liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/50 (2%)	—		Vesselinovitch et al. (1979b)
			Week 1	Gavage, daily	230 µg	Weeks 1–4		5/49 (10%)[d]	—		
			Week 5	Diet, daily	150 ppm	Weeks 5–90		8/49 (16%)[d]	—		
			Week 1	Gavage, daily until 4 weeks, then in diet	230 µg 150 ppm (diet)	Weeks 1–90		10/50 (20%)[c]	—		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Dieldrin	Mice ($B6C3F_1$)	liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/58 (2%)	—		Vesselinovitch et al. (1979b)
			Week 1	Gavage, daily	12.5 µg	Weeks 1–4		3/46 (7%)[b]	—		
			Week 5	Diet, daily	10 ppm	Weeks 5–90		7/60 (12%)[b]	—		
			Week 1	Gavage, daily until 4 weeks, then in diet	12.5 µg 10 ppm	Weeks 1–90		21/70 (30%)[a]	—		
DEN[e] Diethylnitrosamine	Rats (Colworth)	liver	Control		Control	N/A		29/384 (8%)		Highest tumor rate when dosed at earlier ages. Incidents are rats with adenomas or carcinomas.	Peto et al. (1984)
			Week 3	Diet (in drinking water), daily	16 different doses combined[f]	From week 3 until death	6 months–3 years	105/180 (58%)[b]			
			Week 6			From week 6 until death		714/1440 (50%)[b]			
			Week 20			From week 20 until death		76/180 (42%)[b]			
		esophagus	Control		Control	N/A		0/384 (0%)			
			Week 3	Diet (in drinking water), daily	16 different doses combined[g]	From week 3 until death		77/180 (43%)[b]			
			Week 6			From week 6 until death		663/1440 (46%)[b]			
			Week 20			From week 20 until death		88/180 (49%)[b]			

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DPH Diphenylhydantoin, 5,5-	Rats (F344/N)	liver	Control	Control	0 ppm	N/A	2 years	0/50 (0%)	0/50 (0%)	In rats, perinatal exposure ranged from 63 to 630 ppm, and adult exposures ranged from 240 to 2,400 ppm. In mice, perinatal exposure ranged from 21 to 210 ppm. Adult exposure ranged from 30 to 300 ppm in males and 60 to 600 ppm in females. Tumor incidences are animals with adenomas or carcinomas.	Chhabra et al. (1993b)
			Perinatal	Diet, daily	630 ppm	Perinatal through 8 weeks		1/50 (2%)[d]	0/49 (0%)[d]		
			8 weeks		800 ppm	8 weeks–2 years		2/50 (4%)[d]	1/50 (2%)[d]		
			8 weeks		2,400 ppm	8 weeks–2 years		4/50 (8%)[d]	1/50 (2%)[d]		
			Perinatal		630–800	Perinatal through 2 years		1/49 (2%)[d]	0/50 (0%)[d]		
			Perinatal		630–2,400 ppm	Perinatal through 2 years		5/49 (10%)[c]	0/50 (0%)[d]		
	Mice ($B6C3F_1$)	liver	Control	Control male	0 ppm	N/A	2 years	29/50 (58%)			
			Perinatal	Diet, male	210 ppm	Perinatal through 8 weeks		33/50 (66%)[d]			
			8 weeks		100 ppm	8 weeks–2 years		29/49 (59%)[d]			
			8 weeks		300 ppm	8 weeks–2 years		26/49 (53%)[d]			
			Perinatal		210–100 ppm	Perinatal through 2 years		35/49 (71%)[d]			
			Perinatal		210–300 ppm	Perinatal through 2 years		41/50 (82%)[c]			
			Control	Control female	0 ppm	N/A	2 years		5/48 (10.4%)[d]		
			Perinatal	Diet, female	210 ppm	Perinatal through 8 weeks			12/49 (24.5%)[d]		
			8 weeks		200 ppm	8 weeks–2 years			14/49 (28%)[c]		
			8 weeks		600 ppm	8 weeks–2 years			30/50 (60%)[c]		
			Perinatal		210–200 ppm	Perinatal through 2 years			16/50 (32%)[c]		
			Perinatal		210–600 ppm	Perinatal through 2 years			34/50 (68%)[c]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ETU Ethylene thiourea	Rats (F344/N)	thyroid	Control	Control	0 ppm	N/A	2 years	1/49 (2%)	3/50 (6%)	Tumor incidences are animals with adenomas or carcinomas.	Chhabra et al. (1992)
			Perinatal	Diet, daily	90 ppm	Perinatal through 8 weeks		4/49 (8%)[d]	3/50 (6%)[d]		
			8 weeks		83 ppm	8 weeks–2 years		12/46 (26%)[c]	7/44 (16%)[d]		
			8 weeks		250 ppm	8 weeks–2 years		37/50 (74%)[c]	30/49 (61%)[c]		
			Perinatal		90–83 ppm	Perinatal through 2 years		13/50 (26%)[c]	9/47 (19%)[d]		
			Perinatal		90–250 ppm	Perinatal through 2 years		48/50 (96%)	37/50 (74%)		
	Mice ($B6C3F_1$)	liver	Control	Control	0 ppm	N/A	2 years	20/49 (41%)	4/50 (8%)		
			Perinatal	Diet, daily	330 ppm	Perinatal through 8 weeks		13/49 (26.5%)[d]	5/49 (10%)[d]		
			8 weeks		330 ppm	8 weeks–2 years		32/50 (64%)[c]	44/50 (88%)[c]		
			8 weeks		1,000 ppm	8 weeks–2 years		46/50 (92%)[c]	48/50 (96%)[c]		
			Perinatal		330–330 ppm	Perinatal through 2 years		34/49 (69%)[c]	46/50 (92%)[c]		
			Perinatal		330–1,000 ppm	Perinatal through 2 years		47/49 (6%)[c]	49/50 (98%)[c]		
		thyroid	Control	Control	0 ppm	N/A		1/50 (2%)	0/50 (0%)		
			Perinatal	Diet, daily	330 ppm	Perinatal through 8 weeks		1/46 (2%)[d]	1/49 (2%)[d]		
			8 weeks		330 ppm	8 weeks–2 years		1/49 (2%)[d]	2/50 (4%)[d]		
			8 weeks		1,000 ppm	8 weeks–2 years		29/50 (58%)[c]	38/50 (76%)[c]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ETU Ethylene thiourea (continued)			Perinatal		330–330 ppm	Perinatal through 2 years		2/48 (4%)[d]	10/49 (20%)[c]		
			Perinatal		330–1,000 ppm	Perinatal through 2 years		35/49 (71%)[c]	38/50 (76%)[c]		
		pituitary	Control	Control	0 ppm	N/A		0/44 (0%)	11/47 (23%)		
			Perinatal	Diet, daily	330 ppm	Perinatal through 8 weeks		0/42 (0%)[d]	11/48 (23%)[d]		
			8 weeks		330 ppm	8 weeks–2 years		0/42 (0%)[d]	19/49 (39%)[d]		
			8 weeks		1,000 ppm	8 weeks–2 years		8/41 (19.5%)[c]	26/49 (53%)[c]		
			Perinatal		330–330 ppm	Perinatal through 2 years		0/45 (0%)[d]	26/47 (55%)[c]		
			Perinatal		330–1,000 ppm	Perinatal through 2 years		4/39 (10%)[d]	24/47 (51%)[c]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death		Tumor incidence		Reference
							M	F	M	F	
3-Methylcholanthrene (formerly known as 20-methylcholanthrene)	Mice (Albino)	liver	Control	gavage, 3× per week	NA	NA	475 days	480 days	3/39 (7.7%)	0/36 (0%)	Klein (1959)
			8 days		0.25 mg/g	10×	311 days	321 days	21/25 (84%)[b]	7/30 (23.3%)[b]	
			90 days		0.25 mg/g	10×	330 days	366 days	1/26 (3.8%)[b]	0/29 (0%)[d]	
		lung	Control		NA	NA	475 days	480 days	17/39 (43.6%)	14/36 (38.9%)	
			8 days		0.25 mg/g	10×	311 days	321 days	25/25 (100%)[b]	28/30 (93.3%)[b]	
			90 days		0.25 mg/g	10×	330 days	366 days	25/26 (96.2%)[b]	27/29 (93.1%)[b]	
		fore-stomach	Control		NA	NA	475 days	480 days	0/39 (0%)	0/36 (0%)	
			8 days		0.25 mg/g	10×	311 days	321 days	12/25 (48%)[b]	12/30 (40%)[b]	
			90 days		0.25 mg/g	10×	330 days	366 days	13/26 (50%)[b]	8/29 (27.6%)[b]	
		skin	Control		NA	NA	475 days	480 days	0/39 (0%)	0/36 (0%)	
			8 days		0.25 mg/g	10×	311 days	321 days	4/25 (16%)[b]	4/30 (13.3%)[b]	
			90 days		0.25 mg/g	10×	330 days	366 days	1/26 (3.8%)[b]	1/25 (4%)[b]	

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
PBBs Polybrominated biphenyls	Rats (F344/N)	liver[g]	Control	Control	0 ppm	N/A	2 years	1/50 (2%)	0/50 (0%)	Findings suggest that combined perinatal and adult exposure increases PBB-related hepatocellular carcinogenicity relative to adult-only exposure in mice and female rats. Apparent association between increasing incidences of MCL and exposure to PBB in male and female rats. Tumor incidences are animals with adenomas or carcinomas.	Chhabra et al. (1993a)
			Perinatal	Diet	10 ppm	Perinatal–8 weeks		5/50 (10%)[d]	0/50 (0%)[d]		
			8 weeks		10 ppm	8 weeks–2 years		12/49 (24%)[c]	12/50 (24%)[c]		
			8 weeks		30 ppm	8 weeks–2 years		41/50 (82%)[c]	39/50 (78%)[c]		
			Perinatal		10–10 ppm	Perinatal–2 years		16/50 (32%)[c]	39/50 (78%)[c]		
			Perinatal		10–30 ppm	Perinatal–2 years		41/50 (82%)[c]	47/50 (94%)[c]		
		Mono-nuclear cell leukemia (MCL)	Control	Control	0 ppm	N/A	2 years	25/50 (50%)	14/50 (28%)		
			Perinatal	Diet	10 ppm	Perinatal–8 weeks		31/50 (62%)[d]	13/50 (26%)[d]		
			8 weeks		10 ppm	8 weeks–2 years		33/50 (66%)[c]	22/50 (44%)[d]		
			8 weeks		30 ppm	8 weeks–2 years		31/50 (62%)[d]	23/50 (46%)[c]		
			Perinatal		10–10 ppm	Perinatal–2 years		37/50 (74%)[c]	27/50 (54%)[c]		
			Perinatal		10–30 ppm	Perinatal–2 years		37/50 (74%)[c]	25/50 (50%)[c]		
	Mice ($B6C3F_1$)	liver[g]	Control	Control	0 ppm	N/A	2 years	16/50 (32%)	5/50 (10%)		
			Perinatal	Diet	30 ppm	Perinatal–8 weeks		40/50 (80%)[c]	21/50 (42%)[c]		
			8 weeks		10 ppm	8 weeks–2 years		48/49 (98%)[c]	42/50 (84%)[c]		
			8 weeks		30 ppm	8 weeks–2 years		48/50 (96%)[c]	47/48 (98%)[c]		
			Perinatal		10 ppm	Perinatal–2 years		46/49 (94%)[c]	44/50 (88%)[c]		
			Perinatal		30–30 ppm	Perinatal–2 years		50/50 (100%)[c]	47/47 (100%)[c]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Safrole	Mice ($B6C3F_1$)	liver	Control	None	None	N/A	90 weeks	3/100 (3%)	0/100 (0%)	Highest tumor rate in males due to preweaning treatment. Highest tumor rate in females due to susceptibility in adulthood. Tumor incidences are mice with adenomas or carcinomas.	Vesselinovitch et al. (1979b)
			Day 12 of gestation	Gavage, to mothers	120 µg/g body weight	4× (days 12, 14, 16, 18)		2/61 (3%)[d]	0/65 (0%)[d]		
			Newborn	Gavage, to mothers, on alternate days	120 µg/g body weight	From birth until weaning		28/83 (34%)[c]	2/80 (3%)[d]		
			At weaning	Gavage, to offspring, 2× weekly	120 µg/g body weight	From weaning until 90 weeks		4/35 (11%)[d]	22/36 (61%)[c]		
			Day 12 of gestation	Gavage, to mothers, alternate days	120 µg/g body weight	From gestation until weaning		22/68 (32%)[b]	1/72 (1%)[b]		
			Day 12 of gestation	Gavage, to mothers, alternate days until weaning; Gavage, to offspring, 2× weekly	120 µg/g body weight	From gestation until 90 weeks		19/37 (51%)[b]	37/46 (80%)[b]		
Urethane	Mice ($B6AF_1/J$)	liver	1 week	gavage	2.5 mg/pup	1×	39–40 weeks	Tumor incidence[a]		No tumor data for controls.	Klein (1966)
								M	F		
								12/37 (33%)[b]	0/40 (0%)[b]		
			1 week		2.5 mg/pup	16× (1× at 1 week; 3× weekly for 5 weeks beginning at 4 wks of age)	39 weeks	11/33 (33%)[b]	0/31 (0%)[b]		
			4 weeks		2.5 mg/pup	15× (3× weekly for 5 weeks beginning at 4 weeks of age)	41 weeks	0/37 (0%)[b]	0/31 (0%)[b]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
VC Vinyl chloride	Rats (Sprague-Dawley)	liver angio-sarcoma	Control	Control	0 ppm	N/A	135 weeks	0/22 (0%)	0/29 (0%)	Higher tumor risk when exposed at birth, higher for females.	Maltoni et al. (1984)
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	5/18 (28%)[b]	12/24 (50%)[b]		
					10,000 ppm			6/24 (25%)[b]	9/20 (45%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	3/17 (18%)[b]	10/25 (40%)[b]		
					10,000 ppm			3/21 (14%)[b]	4/25 (16%)[b]		
		zymbal gland	Control	Control	0 ppm	N/A	135 weeks	0/28 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	1/12 (8%)[b]	1/17 (6%)[b]		
					10,000 ppm			1/17 (6%)[b]	0/17 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	3/29 (10%)[b]	4/30 (13%)[b]		
					10,000 ppm			10/30 (33%)[b]	6/30 (20%)[b]		
		leukemia	Control	Control	0 ppm	N/A	135 weeks	0/27 (0%)	1/29 (3%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	N/A	1/7 (14%)[b]		
					10,000 ppm			2/6 (33%)[b]	0/15 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	N/A	0/29 (0%)[b]		
					10,000 ppm			0/27 (0%)[b]	2/29 (7%)[b]		
		nephro-blastoma	Control	Control	0 ppm	N/A	135 weeks	0/22 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	0/15 (0%)[b]	0/21 (0%)[b]		
					10,000 ppm			0/19 (0%)[b]	0/17 (0%)[b]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
VC Vinyl chloride (continued)			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	4/18 (22%)[b]	1/26 (4%)[b]		
					10,000 ppm			3/21 (14%)[b]	2/25 (8%)[b]		
		angio-sarcomas: other sites	Control	Control	0 ppm	N/A	135 weeks	0/29 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	1/15 (7%)[b]	0/21 (0%)[b]		
					10,000 ppm			0/19 (0%)	0/17 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	1/29 (3%)[b]	2/30 (7%)[b]		
					10,000 ppm			2/30 (7%)[b]	1/30 (3%)[b]		
		angiomas and fibromas: other sites	Control	Control	0 ppm	N/A	135 weeks	0/28 (0%)	2/29 (7%)[b]		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	1/15 (7%)[b]	0/21 (0%)[b]		
					10,000 ppm			2/19 (11%)[b]	1/17 (6%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	2/29 (7%)[b]	2/30 (7%)[b]		
					10,000 ppm			2/29 (7%)[b]	1/29 (3%)[b]		
		hepatoma	Control	Control	0 ppm	N/A	135 weeks	0/19 (0%)	0/28 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	9/18 (50%)[b]	11/24 (46%)[b]		
					10,000 ppm			13/24 (54%)[b]	7/20 (35%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	0/10 (0%)[b]	1/17 (6%)[b]		
					10,000 ppm			1/8 (13%)[b]	0/16 (0%)[b]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
VC Vinyl chloride (continued)		skin carcinomas	Control	Control	0 ppm	N/A	135 weeks	0/20 (0%)	1/29 (3%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	1/10 (10%)[b]	1/14 (7%)[b]		
					10,000 ppm			1/16 (6%)[b]	0/15 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	0/15 (0%)[b]	2/19 (11%)[b]		
					10,000 ppm			2/13 (15%)[b]	1/21 (5%)[b]		
		neuro-blastoma	Control	Control	0 ppm	N/A	135 weeks	0/22 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	0/18 (0%)[b]	0/29 (0%)[b]		
					10,000 ppm			0/22 (0%)[b]	0/19 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	2/21 (10%)[b]	1/27 (4%)[b]		
					10,000 ppm			2/22 (9%)[b]	5/26 (19%)[b]		

[a] Where not delineated by gender, data combined by study authors or gender not specified. Where percentages only are given, number of subjects not specified.
[b] Not evaluated by authors.
[c] Significant compared with controls.
[d] Evaluated but not significant compared with controls.
[e] Reported as NDEA (N-nitrosodiethylamine) in the original document.
[f] Results from each dose are not available.
[g] Tumors were adenomas or carcinomas.

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
BaP Benzo[*a*]pyrene	Mice ($B6C3F_1$)	liver	Control	Control	None	N/A	142 weeks	7/100 (7%)	1/100 (1%)	In general, hepatomas developed with significantly higher incidence ($p<0.01$) in mice that were treated within 24 hours of birth or at 15 days of age than they did in similarly treated animals at 42 days of age. + higher for males.	Vesselinovitch et al. (1975a)
			Day 1	i.p.	75 µg/g body weight	1×	86 weeks (m) 129 weeks (f)	26/47 (55%)[b]	3/45 (7%)[b]		
					150 µg/g body weight	1×	81 weeks (m) 121 weeks (f)	51/63 (81%)[b]	8/45 (18%)[b]		
			Day 15	i.p.	75 µg/g body weight	1×	93 weeks (m) 116 weeks (f)	36/60 (60%)[b]	4/55 (7%)[b]		
					150 µg/g body weight	1×	81 weeks (m) 90 weeks (f)	32/55 (58%)[b]	4/55 (7%)[b]		
			Day 42	i.p.	75 µg/g body weight	1×	108 weeks(m)	7/55 (13%)[b]	0/47 (0%)[b]		
					150 µg/g body weight	1×	87 weeks (m)	4/47 (9%)[b]	0/46 (0%)[b]		
	Mice ($C3AF_1$)	liver	Control	Control	None	N/A	142 weeks	8/100 (8%)	1/100 (1%)	+ higher for males. “Age at death” is the average age at which tumors were observed.	
			Day 1	i.p.	75 µg/g body weight	1×	80 weeks (m) 91 weeks (f)	21/62 (34%)[b]	1/45 (2%)[b]		
					150 µg/g body weight	1×	69 weeks (m) 701 weeks (f)	24/52 (46%)[b]	1/56 (2%)[b]		
			Day 15	i.p.	75 µg/g body weight	1×	90 weeks (m) 102 weeks (f)	15/56 (27%)[b]	1/49 (2%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
BaP Benzo[*a*]pyrene (continued)					150 µg/g body weight	1×	77 weeks (m) 62 weeks (f)	12/53 (23%)[b]	1/57 (2%)[b]		
			Day 42	i.p.	75 µg/g body weight	1×		0/30 (0%)[b]	0/32 (0%)[b]		
					150 µg/g body weight	1×	79 weeks (m)	1/32 (3%)[c]	0/40 (0%)[b]		
	Mice ($B6C3F_1$)	lung	Control	Control	Control	N/A	142 weeks	13/100 (13%)	9/100 (9%)	Both sexes developed lung tumors with higher incidence when treated with BaP at birth than at 15 or 42 days of age ($p<0.05$).	
			Day 1	i.p.	75 µg/g body weight	1×	103 weeks (m) 126 weeks (f)	20/47 (43%)[b]	22/45 (49%)[b]		
					150 µg/g body weight	1×	84 weeks (m) 112 weeks (f)	37/63 (59%)[b]	28/45 (62%)[b]		
			Day 15	i.p.	75 µg/g body weight	1×	103 weeks (m) 122 weeks (f)	15/60 (25%)[b]	18/55 (33%)[b]		
					150 µg/g body weight	1×	82 weeks (m) 101 weeks (f)	20/55 (36%)[b]	18/45 (40%)[b]		
			Day 42	i.p.	75 µg/g body weight	1×	119 weeks (m) 131 weeks (f)	20/55 (36%)[b]	12/47 (26%)[b]		
					150 µg/g body weight	1×	95 weeks (m) 118 weeks (f)	18/47 (38%)[b]	8/46 (17%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
BaP Benzo[*a*]pyrene (continued)	Mice ($C3AF_1$)	lung	Control	Control	None	N/A	142 weeks	60/100 (60%)	50/100 (50%)	Of the two mouse strains tested, $C3AF_1$ mice developed significantly more tumors than did the $B6C3F_1$ mice ($p<0.001$).	Vesselinovitch et al. (1975a)
			Day 1	i.p.	75 µg/g body weight	1×	78 weeks (m) 82 weeks (f)	58/62 (93%)[b]	42/45 (93%)[b]		
					150 µg/g body weight	1×	70 weeks (m) 73 weeks (f)	48/52 (92%)[b]	52/56 (93%)[b]		
			Day 15	i.p.	75 µg/g body weight	1×	87 weeks (m) 98 weeks (f)	52/56 (93%)[b]	46/49 (94%)[b]		
					150 µg/g body weight	1×	75 weeks (m) 79 weeks (f)	50/53 (94%)[b]	52/57 (91%)[b]		
			Day 42	i.p.	75 µg/g body weight	1×	91 weeks (m) 93 weeks (f)	28/30 (93%)[b]	28/32 (87%)[b]		
					150 µg/g body weight	1×	85 weeks (m) 83 weeks (f)	28/32 (87%)[b]	36/40 (90%)[b]		
DBA Dibenzanthracene	Mice (Caracul × P stock)	lung	Control	Control	None	N/A	228 days	1/31 (3.2%)			Law (1940)
			Day 1	i.p.	4 mg per cm^3 vehicle	1×	181 days	24/24 (100%)[b]			
			2 months	s.c.	4 mg per cm^3 vehicle	1×	189 days	2/29 (6.9%)[b]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine	Mice ($B6C3F_1$)	liver	Control	Control	Vehicle (0.01 mL trioctanoin/g body weight)	4×	142 weeks (m) 137 weeks (f)	7/98 (7%)	1/100 (1%)	Animals treated as newborns and infants developed significantly more liver tumors than animals that were treated as young adults. Newborns and infant females developed liver tumors at a later age than similarly treated males. Incidences for malignant tumors only.	Vesselinovitch et al. (1984)
			Day 1	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×	67 weeks (m) 90 weeks (f)	37/51 (73%)[b]	45/64 (70%)[b]		
					3 µg/g body weight	4×	65 weeks (m) 80 weeks (f)	40/58 (69%)[b]	44/65 (68%)[b]		
			Day 15		1.5 µg/g body weight	4×	86 weeks (m) 117 weeks (f)	41/57 (72%)[b]	40/71 (56%)[b]		
					3 µg/g body weight	4×	76 weeks (m) 96 weeks (f)	48/69 (70%)[b]	46/62 (74%)[b]		
			Day 42		1.5 µg/g body weight	4×	117 weeks (m) 135 weeks (f)	9/49 (18%)[b]	1/47 (2%)[b]		
					3 µg/g body weight	4×	123 weeks (m) 133 weeks (f)	6/38 (16%)[b]	4/57 (7%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine (continued)	Mice ($C3AF_1$)	liver	Control	Control	Vehicle (0.1 trioctanoin/g body weight)	4×	123 weeks (m) 131weeks (f)	8/99 (8%)	1/97 (1%)	Highest tumor rate when dosed at early ages. Newborns and infant females developed liver tumors at a lower incidence than similarly treated males. + higher for males.	Vesselinovitch et al. (1984)
			Day 1	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×	64 weeks (m) 84 weeks (f)	23/32 (72%)[b]	11/39 (28%)[b]		
					3 µg/g body weight	4×	59 weeks (m) 76 weeks (f)	39/58 (67%)[b]	26/50 (52%)[b]		
			Day 15		1.5 µg/g body weight	4×	82 weeks (m) 102 weeks (f)	22/46 (48%)[b]	8/65 (12%)[b]		
					3 µg/g body weight	4×	74 weeks (m) 94 weeks (f)	35/54 (65%)[b]	22/62 (35%)[b]		
			Day 42		1.5 µg/g body weight	4×	105 weeks (m) 106 weeks (f)	12/56 (22%)[b]	0/53 (0%)[b]		
					3 µg/g body weight	4×	105 weeks (m) 103 weeks (f)	9/57 (16%)[b]	0/56 (0%)[b]		
	Mice ($B6C3F_1$)	lung	Control	Control	Vehicle (0.1 trioctanoin/g body weight)	4×	142 weeks (m) 137 weeks (f)	13/98 (13%)	9/100 (9%)	The mice treated as newborns showed lung tumors earlier than animals exposed at other times. It is not known whether this was due to actual earlier emergence of tumors or	

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine (continued)			Day 1	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×	70 weeks (m) 91 weeks (f)	29/51 (57%)[b]	49/64 (77%)[b]	to their earlier detection caused by shorter survival.	
					3 µg/g body weight	4×	68 weeks (m) 81 weeks (f)	34/58 (59%)[b]	42/65 (65%)[b]		
			Day 15		1.5 µg/g body weight	4×	87 weeks (m) 115 weeks (f)	51/57 (89%)[b]	61/71 (86%)[b]		
					3 µg/g body weight	4×	77 weeks (m) 97 weeks (f)	51/69 (74%)[b]	53/62 (85%)[b]		
			Day 42		1.5 µg/g body weight	4×	123 weeks (m) 129 weeks (f)	38/49 (78%)[b]	38/47 (81%)[b]		
					3 µg/g body weight	4×	121 weeks (m) 127 weeks (f)	33/38 (87%)[b]	43/57 (75%)[b]		
	Mice ($C3AF_1$)	lung	Control	Control	Vehicle (0.1 trioctanoin/g body weight)	4×	142 weeks (m) 137weeks (f)	60/99 (61%)	50/97 (52%)	Of the two strains, $C3AF_1$ mice developed lung tumors with a higher incidence and multiplicity than $B6C3F_1$ hybrids.	
			Day 1	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×	65 weeks (m) 84 weeks (f)	30/32 (94%)[b]	38/39 (97%)[b]		
					3 µg/g body weight	4×	59 weeks (m) 76 weeks (f)	49/58 (84%)[b]	46/50 (92%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine (continued)			Day 15		1.5 µg/g body weight	4×	80 weeks (m) 101 weeks (f)	42/46 (91%)[b]	61/65 (94%)[b]		
					3 µg/g body weight	4×	74 weeks (m) 92 weeks (f)	50/54 (93%)[b]	57/62 (92%)[b]		
			Day 42		1.5 µg/g body weight	4×	104 weeks (m) 110 weeks (f)	55/56 (98%)[b]	52/53 (98%)[b]		
					3 µg/g body weight	4×	101 weeks (m) 102 weeks (f)	56/57 (98%)[b]	54/56 (96%)[b]		
	Mice ($B6C3F_1$)	liver	Control	Control	None	N/A	90 weeks	1/98 (1%)	0/96 (0%)	Infant animals of both sexes (Day 15) were more sensitive than similarly exposed adults.	Vesselinovitch and Mihailovich (1983)
			Gestation day 18	i.p.	1.5 µg/g body weight	1×		2/50 (4%)[b]	1/51 (2%)[b]		
			Day 15	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×		47/51 (92%)[b]	60/64 (94%)[b]		
			Day 42		1.5 µg/g body weight	4×		13/49 (26%)[b]	3/47 (6%)[b]		
			Day 1	i.p.	1.5 µg/g body weight	1×	73 weeks	15/59 (25%)[b]	—	At the 1.5-µg dose level, 1-day-old mice developed significantly fewer liver tumors than similarly treated infants (Day 15) ($p<0.025$). Tumor incidence in treated groups versus controls was not evaluated.	Vesselinovitch et al. (1979a)
					5 µg/g body weight	1×		29/45 (64%)[b]	—		
					10 µg/g body weight	1×		24/25 (96%)[b]	—		
			Day 15	i.p.	1.5 µg/g body weight	1×		13/24 (54%)[b]	—		
					5 µg/g body weight	1×		40/54 (74%)[b]	—		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine (continued)					10 µg/g body weight	1×		25/25 (100%)[b]	—		
DMBA Dimethyl-benz[*a*]anthracene	Rats (Sprague-Dawley)	mammary adeno-sarcoma	Day 20	Gavage	10 mg/100 g body weight	1×	Week 25	—	3/6 (50%)[b]	36 of 42 (86%) animals dosed at age 20 days died soon after. Highest number of tumors per animal was in the 46-day group, with decreasing numbers in the older animals. Animals were sacrificed 22 weeks after treatment.	Russo et al. (1979)
			Day 30		10 mg/100 g body weight	1×	Week 26	—	14/15 (93%)[b]		
			Day 40		10 mg/100 g body weight	1×	Week 27	—	8/9 (89%)[b]		
			Day 46		10 mg/100 g body weight	1×	Week 28	—	8/8 (100%)[b]		
			Day 55		10 mg/100 g body weight	1×	Week 29	—	33/34 (97%)[b]		
			Day 70		10 mg/100 g body weight	1×	Week 32	—	5/8 (63%)[b]		
			Day 140		10 mg/100 g body weight	1×	Week 42	—	10/15 (67%)[b]		
			Day 180		10 mg/100 g body weight	1×	Week 47	—	14/26 (54%)[b]		
	Rats (Wistar)	mammary carcinoma[d]	Control 5–8 weeks	Control	None	N/A	17 months	0/22 (0%)	0/25 (0%)	Highest tumor rate in females exposed at 5–8 weeks. Animals were observed for 16 months following treatment.	Meranze et al. (1969)
			Control 26 weeks	Control	None	N/A	20 months	0/31 (0%)	2/20 (10%)		
			< Week 2	Gavage	0.5–1.0 mg	1×	Week 40–56	0/23 (0%)[b]	4/50 (8%)[b]		
			Week 5–8		15 mg	1×	Week 14–55	0/23 (0%)[b]	14/25 (56%)[b]		
			Week 26		15 mg	1×	Week 32–73	0/34 (0%)[b]	4/26 (15%)[b]		
	Rats (Wistar, castrated)	mammary carcinoma	Week 5–8	Gavage	15 mg	1×	Week 14–55	0/21 (0%)[b]	0/22 (0%)[b]		
			Week 26		15 mg	1×	Week 32–73	0/33 (0%)[b]	0/26 (0%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DMBA Dimethyl-benz[*a*]anthracene (continued)	Rats (Wistar)	Total tumors	Control 5–8 weeks	Control	None	N/A	17 months	0/22 (0%)	0/25 (0%)	Total tumors includes leukemia.	
			Control 26 weeks	Control	None	N/A	20 months	2/31 (6%)	5/20 (25%)		
			< Week 2	Gavage	0.5–1.0 mg	1×	Week 40–56	16/23 (70%)[b]	36/50 (72%)[b]		
			Week 5–8		15 mg	1×	Week 14–55	7/23 (30%)[b]	16/25 (64%)[b]		
			Week 26		15 mg	1×	Week 32–73	12/34 (35%)[b]	13/26 (50%)[b]		
	Mice (BALB/c)	lung	Control: Day 1	Control s.c.	Aqueous gelatine	1×	40 weeks	0/12 (0%)	7/23 (30%)	15 µg DMBA gave rise to a significantly greater incidence of lung tumors when administered to newborn mice than to suckling or young adults.	Walters (1966)
			Day 1	s.c.	15 µg	1×	40 weeks[f]	14/14 (100%)[b]	24/24 (100%)[b]		
			Week 2–3 (suckling)	s.c.	15 µg	1×	42–43 weeks	12/23 (52%)[b]	16/22 (73%)[b]		
				s.c.	30 µg (60 µg total)	2×	42–43 weeks	14/14 (100%)[b]	24/24 (100%)[b]		
			Adult[e]	s.c.	15 µg	1×	48-49 weeks	6/12 (50%)[b]	15/33 (45%)[b]		
				s.c.	30 µg (60 µg total)	2×	48-49 weeks	9/10 (90%)[b]	21/23 (91%)[b]		
				s.c.	30 µg (180 µg total)	6×	48-49 weeks	12/12 (100%)[b]	13/13 (100%)[b]		
	Mice (Swiss)	lymphoma	Control	Control	None	N/A	31–52 weeks	3/408 (0.7%)		Higher tumor rates at younger age of exposure. Only one treatment group was exposed i.p.; others were exposed by s.c. injection..	Pietra et al. (1961)
			Day 1	i.p.	30–40 µg	1×	13–33 weeks	6/31 (19%)[b]			
			Day 1	s.c.	30–40 µg	1×	12–27 weeks	8/27 (30%)[b]			
			Week 8	s.c.	900 µg	1×	30 weeks	1/13 (8%)[b]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DMBA Dimethyl-benz[*a*]anthracene (continued)	Mice (Swiss)	lung	Control	Control	None	N/A	31–52 weeks	4/408 (0.9%)			
			Day 1	i.p.	30–40 µg	1×	13–33 weeks	24/31 (77%)[b]			
			Day 1	s.c.	30–40 µg	1×	12–27 weeks	23/27 (85%)[b]			
			Week 8	s.c.	900 µg	1×	30 weeks	2/13 (15%)[b]			
DMN Dimethyl-nitrosamine	Rats (Wistar)	kidney carcinoma	Day 1	i.p.	20 mg/kg	1×	≥5 months	1/33 (3)[b]		In the neonatal group, the dose was reduced to 20 mg/kg to achieve approximately equivalent numbers of survivors. No control group.	Hard (1979)
			Day 21		30 mg/kg	1×		5/39 (13)[b]			
			Month 1		30 mg/kg	1×		2/33 (6)[b]			
			Month 1.5		30 mg/kg	1×		1/28 (4)[b]			
			Month 2		30 mg/kg	1×		1/26 (4)[b]			
			Month 3		30 mg/kg	1×		10/27 (37)[b]			
			Month 4		30 mg/kg	1×		7/32 (22)[b]			
			Month 5		30 mg/kg	1×		0/14 (0)[b]			
	Rats (Wistar)	kidney adenoma	Day 1	i.p.	20 mg/kg	1×	≥5 months	1/33 (3)[b]			
			Day 21		30 mg/kg	1×		13/39 (33)[b]			
			Month 1		30 mg/kg	1×		11/33 (33)[b]			
			Month 1.5		30 mg/kg	1×		13/28 (48)[b]			
			Month 2		30 mg/kg	1×		11/26 (42)[b]			
			Month 3		30 mg/kg	1×		18/27 (67)[b]			
			Month 4		30 mg/kg	1×		17/32 (53)[b]			
			Month 5		30 mg/kg	1×		6/14 (43)[b]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DMN Dimethyl-nitrosamine (continued)	Rats (Wistar)	kidney mesenchymal tumors	Day 1	i.p.	20 mg/kg	1×	≥5 months	8/33 (24)[b]		Mesenchymal tumors were most frequent in the three youngest age groups (z test, $p < 0.001$).	
			Day 21		30 mg/kg	1×		18/39 (46)[b]			
			Month 1		30 mg/kg	1×		23/33 (70)[b]			
			Month 1.5		30 mg/kg	1×		5/28 (19)[b]			
			Month 2		30 mg/kg	1×		2/26 (8)[b]			
			Month 3		30 mg/kg	1×		3/27 (11)[b]			
			Month 4		30 mg/kg	1×		7/32 (22)[b]			
			Month 5		30 mg/kg	1×		0/14 (0)[b]			
	Rats (Wistar)	kidney cortical epithelial tumors	Day 1	i.p.	20 mg/kg	1×	≥5 months	2/33 (6)[b]			Hard (1979)
			Day 21		30 mg/kg	1×		16/39 (41)[b]			
			Month 1		30 mg/kg	1×		12/33 (36)[b]			
			Month 1.5		30 mg/kg	1×		14/28 (52)[b]			
			Month 2		30 mg/kg	1×		11/26 (42)[b]			
			Month 3		30 mg/kg	1×		18/27 (67)[b]			
			Month 4		30 mg/kg	1×		21/32 (66)[b]			
			Month 5		30 mg/kg	1×		6/14 (43)[b]			
	Rats (Wistar)	Total tumors	Day 1	i.p.	20 mg/kg	1×	≥5 months	11/33 (33)[b]			
			Day 21		30 mg/kg	1×		25/39 (64)[b]			
			Month 1		30 mg/kg	1×		25/33 (76)[b]			
			Month 1.5		30 mg/kg	1×		17/28 (63)[b]			
			Month 2		30 mg/kg	1×		13/26 (50)[b]			
			Month 3		30 mg/kg	1×		18/27 (67)[b]			
			Month 4		30 mg/kg	1×		22/32 (69)[b]			
			Month 5		30 mg/kg	1×		7/14 (50)[b]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ENU Ethylnitrosourea	Rats	nervous system	Day 1	Injection	20 mg/kg	1×		100%[b]		Susceptibility to neuro-oncogenic effect declined with increasing age.	Maekawa and Mitsumori (1990)
			Day 30	Injection	20 mg/kg	1×		61%[b]			
	Mice ($B6C3F_1$)	liver	Control	Control	None	N/A	90 weeks	1/98 (1%)	0/96 (0%)	Both male and female mice were responsive to exposure during prenatal and infant life.	Vesselinovitch (1983)
			Gestation day 18	i.p.	60 µg/g body weight	1×		28/52 (54%)[b]	18/49 (37%)[b]		
			Day 15		60 µg/g body weight	1×		41/50 (82%)[b]	28/51 (55%)[b]		
			Day 42		60 µg/g body weight	1×		10/50 (20%)[b]	5/50 (10%)[b]		
	Rats (Wistar)	nerve tissue	Control	Control	None	N/A	4–7 months	0/16 (0%)	0/10 (0%)	Highest tumor rate seen when exposed during gestation or soon after birth. Statistically significant decrease in tumor incidence with increasing age of exposure.	Naito et al. (1981)
			Gestation day 16	i.p.	40 mg/kg	1×		26/26 (100%)[b]	18/18 (100%)[b]		
			Day 1	s.c.	40 mg/kg	1×		12/12 (100%)[g]	16/16 (100%)[g]		
			Week 1		40 mg/kg	1×		12/17 (71%)[b]	18/20 (90%)[b]		
			Week 2		40 mg/kg	1×		10/14 (71%)[b]	14/18 (78%)[b]		
			Week 3		40 mg/kg	1×		6/13 (46%)[b]	5/17 (29%)[b]		
			Week 4		40 mg/kg	1×		8/15 (53%)[b]	2/10 (20%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ENU Ethylnitrosourea (continued)	Mice ($B6C3F_1$)	lung	Day 1	i.p.	60 µg/g body weight	1×		49/55 (89%)[b]	49/50 (98%)[b]		Vesselinovitch et al. (1974)
			Day 15			1×		50/55 (91%)[b]	47/55 (85%)[b]		
			Day 42			1×		53/59 (90%)[b]	44/51 (86%)[b]		
			Day 1		120 µg/g body weight	1×		36/38 (95%)[b]	54/60 (90%)[b]		
			Day 15			1×		45/49 (92%)[b]	43/50 (86%)[b]		
			Day 42			1×		52/54 (96%)[b]	50/57 (88%)[b]		
	Mice ($C3AF_1$)	lung	Day 1		60 µg/g body weight	1×		46/47 (98%)[g]	51/51 (100%)[g]		
			Day 15			1×		49/49 (100%)[g]	57/59 (97%)[g]		
			Day 42			1×		59/59 (100%)[g]	57/57 (100%)[g]		
			Day 1		120 µg/g body weight	1×		63/64 (98%)[g]	53/57 (93%)[g]		
			Day 15			1×		54/56 (96%)[g]	50/56 (89%)[g]		
			Day 42			1×		59/59 (100%)[g]	48/48 (100%)[g]		
	Mice ($B6C3F_1$)	liver	Day 1	i.p.	60 µg/g body weight	1×		50/54 (93%)[g]	28/43 (65%)[g]		
			Day 15			1×		55/56 (98%)[g]	33/54 (61%)[g]		
			Day 42			1×		12/40 (30%)[b]	6/39 (15%)[b]		
			Day 1		120 µg/g body weight	1×		29/34 (85%)[g]	32/53 (60%)[g]		
			Day 15			1×		45/48 (94%)[g]	29/43 (67%)[g]		
			Day 42			1×		17/49 (35%)[g]	4/50 (8%)[g]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ENU Ethylnitrosourea (continued)	Mice ($C3AF_1$)	liver	Day 1	i.p.	60 µg/g body weight	1×		42/45 (93%)[g]	19/41 (46%)[g]		
			Day 15			1×		42/50 (84%)[g]	19/48 (40%)[g]		
			Day 42			1×		7/29 (24%)[b]	4/50 (8%)[b]		
			Day 1		120 µg/g body weight	1×		55/62 (89%)[g]	19/45 (42%)[g]		
			Day 15			1×		35/45 (78%)[g]	15/35 (43%)[g]		
			Day 42			1×		8/33 (24%)[b]	3/33 (9%)[b]		
	Mice ($B6C3F_1$)	kidney	Day 1	i.p.	60 µg/g body weight	1×		11/48 (23%)[b]	5/49 (10%)[b]		
			Day 15			1×		6/41 (15%)[b]	7/31 (23%)[b]		
			Day 42			1×		4/40 (10%)[b]	3/37 (8%)[b]		
			Day 1		120 µg/g body weight	1×		10/30 (33%)[g]	14/53 (26%)[b]		
			Day 15			1×		17/37 (46%)[g]	19/49 (39%)[b]		
			Day 42			1×		8/40 (20%)[b]	11/39 (28%)[b]		
	Mice ($C3AF_1$)	kidney	Day 1	i.p.	60 µg/g body weight	1×		7/44 (16%)[b]	6/45 (13%)[b]		
			Day 15			1×		7/41 (17%)[b]	8/46 (17%)[b]		
			Day 42			1×		3/42 (42%)[b]	3/43 (7%)[b]		
			Day 1		120 µg/g body weight	1×		4/52 (7%)[b]	6/29 (21%)[g]		
			Day 15			1×		8/35 (23%)[b]	12/29 (41%)[g]		
			Day 42			1×		6/41 (71%)[b]	3/39 (8%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ENU Ethylnitrosourea (continued)	Mice (B6C3F1)	Harderian	Day 1		60 µg/g body weight	1×		7/40 (17%)[b]	5/43 (12%)[b]		
			Day 15			1×		10/51 (20%)[b]	17/59 (29%)[b]		
			Day 42			1×		14/50 (28%)[b]	14/45 (31%)[b]		
			Day 1		120 µg/g body weight	1×		9/30 (30%)[g]	6/52 (12%)[b]		
			Day 15			1×		15/41 (37%)[g]	8/31 (26%)[b]		
			Day 42			1×		25/48 (52%)[g]	14/49 (29%)[b]		
	Mice ($C3AF_1$)	Harderian	Day 1		60 µg/g body weight	1×		3/25 (12%)[b]	4/35 (11%)[b]		
			Day 15			1×		1/9 (11%)[b]	6/38 (16%)[b]		
			Day 42			1×		12/48 (25%)[b]	5/33 (15%)[b]		
			Day 1		120 µg/g body weight	1×		3/52 (6%)[b]	1/25 (4%)[b]		
			Day 15			1×		6/46 (13%)[b]	2/52 (4%)[b]		
			Day 42			1×		5/29 (17%)[b]	2/11 (18%)[b]		
	Mice ($B6C3F_1$)	stomach	Day 1		60 µg/g body weight	1×		3/48 (6%)[b]	4/43 (9%)[b]		
			Day 15			1×		10/42 (24%)[g]	7/45 (16%)[b]		
			Day 42			1×		9/51 (18%)[g]	8/36 (22%)[b]		
			Day 1		120 µg/g body weight	1×		2/29 (7%)[b]	9/53 (17%)[b]		
			Day 15			1×		10/35 (29%)[g]	12/33 (36%)[b]		
			Day 42			1×		12/53 (23%)[g]	12/50 (24%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ENU Ethylnitrosourea (continued)	Mice ($C3AF_1$)	stomach	Day 1		60 µg/g body weight	1×		2/39 (5%)[b]	7/45 (16%)[b]		
			Day 15			1×		7/45 (16%)[g]	7/38 (18%)[b]		
			Day 42			1×		14/55 (25%)[g]	7/49 (14%)[b]		
			Day 1		120 µg/g body weight	1×		8/60 (13%)[b]	9/44 (20%)[b]		
			Day 15			1×		16/51 (31%)[g]	11/42 (26%)[b]		
			Day 42			1×		19/48 (40%)[g]	13/37 (35%)[b]		
	Mice ($B6C3F_1$)	malignant lymphomas	Day 1		60 µg/g body weight	1×		2/55 (4%)[b]	6/52 (12%)[g]		
			Day 15			1×		3/56 (5%)[b]	14/59 (24%)[g]		
			Day 42			1×		9/59 (15%)[b]	17/59 (29%)[g]		
			Day 1		120 µg/g body weight	1×		8/39 (20%)[b]	15/65 (23%)[g]		
			Day 15			1×		14/60 (23%)[b]	17/58 (29%)[g]		
			Day 42			1×		12/59 (20%)[b]	14/60 (23%)[g]		
	Mice ($C3AF_1$)	malignant lymphomas	Day 1		60 µg/g body weight	1×		6/49 (12%)[b]	8/49 (16%)[g]		
			Day 15			1×		3/49 (6%)[b]	13/61 (21%)[g]		
			Day 42			1×		6/60 (10%)[b]	9/55 (16%)[g]		
			Day 1		120 µg/g body weight	1×		3/66 (5%)[b]	10/58 (17%)[g]		
			Day 15			1×		10/56 (18%)[b]	18/60 (30%)[g]		
			Day 42			1×		3/49 (6%)[b]	13/50 (26%)[g]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
NMU Methylnitrosourea	Mice ($BC3F_1$)	Total tumors	Control	Control	N/A	N/A	60 weeks	1/20 (5%)	0%	Control mice did not exhibit tumors in target sites except a single hepatoma in a male control mouse.	Terracini and Testa (1970)
		lung	Day 1	i.p.	50 µg/g body weight	1×	60 weeks	12/15 (80%)[b]	16/19 (84%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	10/26 (39%)[b]	10/35 (29%)[b]		
		lympho-sarcoma	Day 1		50 µg/g body weight	1×	60 weeks	23/39 (59%)[b]	23/45 (51%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	11/35 (31%)[b]	21/45 (47%)[b]		
		liver	Day 1		50 µg/g body weight	1×	60 weeks	10/12 (83%)[b]	1/17 (6%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	0%[b]	0%[c]		
		kidney	Day 1		50 µg/g body weight	1×	60 weeks	3/15 (20%)[b]	3/18 (17%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	2/21 (10%)[b]	0%[c]		
		fore-stomach	Day 1		50 µg/g body weight	1×	60 weeks	0%[b]	4/17 (24%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	8/22 (36%)[b]	12/18 (67%)[b]		
	Rats (Wistar)	mammary	Day 1	i.p.	50 µg/g body weight	1×	60 weeks	0%[b]	4/14 (29%)[b]	Tumor incidence for control rats was based on previous experiments (Della Porta et al., 1968) and was not specifically reported in this paper.	Terracini and Testa (1970)
			5 weeks		50 µg/g body weight	1×	60 weeks	0%[b]	3/5 (60%)[b]		
		lympho-sarcoma	Day 1		50 µg/g body weight	1×	60 weeks	1/10 (10%)[b]	0%[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	2/8 (25%)[b]	1/11 (9%)[b]		
		kidney (ana-plastic)	Day 1		50 µg/g body weight	1×	60 weeks	14/18 (78%)[b]	9/13 (69%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	2/5 (40%)[b]	5/12 (42%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
NMU Methylnitrosourea (continued)		kidney (adenoma)	Day 1		50 µg/g body weight	1×	60 weeks	3/14 (21%)[b]	2/6 (33%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	¼ (25%)[b]	0%[b]		
		forestomach	Day 1		50 µg/g body weight	1×	60 weeks	4/14 (29%)[b]	3/6 (50%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	0%[c]	0%[b]		
		intestine	Day 1		50 µg/g body weight	1×	60 weeks	3/10 (30%)[b]	2/2 (100%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	2/4 (50%)[b]	0%[b]		
	Mice (C3Hf/Dp)	thymus	control	i.p.	NA	NA	120 wks[**]	0/34 (0%)	0/25 (0%)	[*]Age at death from thymic lymphoma reported specifically for some, but not all, dose groups. [**]Control mice were sacrificed at 120 wks. [***]Age of death for all mice in this dose group, regardless of cancer type.	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	29 ± 8.4 wks	2/16 (13%)[b]	5/25 (20%)[b]		
			Day 70		25 µg NMU/g body weight	1×	120 wks (M)[***] 100 wks (F)	0/20 (0%)[c]	1/20 (5%)[b]		
			Day 1		50 µg NMU/g body weight	1×	16.5 ± 0.7 wks	16/24 (67%)[b]	30/44 (68%)[b]		
			Day 21		50 µg NMU/g body weight	1×	24.5 ± 2.5 wks	14/44 (32%)[b]	18/38 (47%)[b]		
			Day 70		50 µg NMU/g body weight	1×	31.4 ± 4.4 wks	9/30 (30%)[b]	6/41 (15%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death		Tumor incidence		Reference
							M	F	M	F	
NMU Methylnitrosourea (continued)	Mice (C3Hf/Dp)	extra-thymic lymphoma	control	i.p.	NA	NA	120 weeks	120 weeks	1/34 (3%)	2/25 (8%)	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	2/16 (13%)[b]	1/25 (4%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	0/20 (0%)[b]	0/20 (0%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	0/24 (0%)[b]	0/44 (0%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	1/44 (2%)[b]	0/38 (0%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	1/30 (3%)[b]	0/41 (0%)[b]	
		lung	control	i.p.	NA	NA	120 weeks	120 weeks	4/34 (12%)	6/25 (24%)	
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	7/16 (44%)[b]	13/25 (52%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	12/20 (60%)[b]	8/20 (40%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	5/24 (21%)[b]	11/44 (25%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	23/44 (52%)[b]	15/38 (39%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	18/30 (60%)[b]	24/41 (59%)[b]	
		liver	control	i.p.	NA	NA	120 weeks	120 weeks	13/34 (38%)	1/25 (4%)	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	9/16 (56%)[g]	2/25 (8%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	12/20 (60%)[g]	2/20 (10%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	4/24 (17%)[g]	3/44 (7%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	21/44 (48%)[g]	1/38 (2.6%)[b]	

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death		Tumor incidence		Reference
							M	F	M	F	
NMU Methylnitrosourea (continued)	Mice (C3Hf/Dp)		Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	8/30 (27%)[g]	2/41 (5%)[b]	
		stomach	control	i.p.	NA	NA	120 weeks	120 weeks	0/34 (0%)	5/25 (20%)	
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	2/16 (13%)[b]	10/25 (40%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	3/20 (15%)[b]	7/20 (35%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	2/24 (8%)[b]	1/44 (2%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	19/44 (43%)[b]	9/38 (24%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	8/30 (27%)[b]	21/41 (51%)[b]	
		kidney	control	i.p.	NA	NA	120 weeks	120 weeks	0/34 (0%)	0/25 (0%)	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	0/16 (0%)[b]	0/25 (0%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	0/20 (0%)[b]	0/20 (0%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	0/24 (0%)[b]	4/44 (9%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	1/44 (2%)[b]	4/38 (11%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	5/30 (17%)[b]	7/41 (17%)[b]	

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death		Tumor incidence		Reference
							M	F	M	F	
NMU Methylnitrosourea (continued)	Mice (C3Hf/Dp)	ovary	control	i.p.	NA	NA	120 weeks	120 weeks	NA	3/25 (12%)	
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	2/25 (8%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	NA	4/20 (20%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	NA	0/44 (0%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	9/38 (24%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	NA	16/41 (39%)[b]	
		mammary	control	i.p.	NA	NA	120 weeks	120 weeks	NA	2/25 (8%)	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	1/25 (4%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	NA	0/20 (0%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	NA	0/44 (0%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	1/44 (2%)[b]	0/38 (0%)[b]	
			Day 70		50 µg NMU/g body weight		110 weeks	90 weeks	NA	4/41 (9.8%)[b]	
		uterus or vagina	control	i.p.	NA	NA	120 weeks	120 weeks	NA	1/25 (4%)	
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	1/25 (4%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	NA	6/20 (30%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	NA	0/44 (0%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	1/38 (3%)[b]	
			Day 70		50 µg NMU/g body weight		110 weeks	90 weeks		7/41 (17%)[b]	

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Urethane	Mice (SWR)	lung adenoma	Newborn	s.c.	0.18 mg/g body weight	1×	10 weeks	100%[b]		The average number of tumors per mouse increased linearly with dose.	Kaye and Trainin (1966)
			11–22 weeks	s.c.	0.25 mg/g body weight	1×	23–34 weeks	0%[b]			
	Mice (C3H/f)	liver	Control	Control	None	N/A	493 days (m) 553 days (f)	14/97 (14%)	1/77 (1%)		Liebelt et al. (1964)
			Day 1	i.p.	0.8 mg/g body weight	1×	481 days (m) 434 days (f)	27/30 (90%)[g]	18/39 (46%)[g]		
			8–10 weeks	i.p.	1 mg/g body weight	1×	321 days (m) -	6/25 (24%)[c]	0/32 (0%)[c]		
		lung	Control	Control	None	N/A	493 days (m) 553 days (f)	0/97 (0%)	0/77 (0%)	The number of lung tumors among the controls was not provided.	
			Day 1	i.p.	0.8 mg/g body weight	1×	401 days (m) 408 days (f)	14/30 (46%)[g]	19/39 (48%)[g]		
			8–10 weeks	i.p.	1 mg/g body weight	1×	506 days (m) -	2/25 (8%)[c]	0/32 (0%)[c]		
		reticular tissue	Control	Control	None	N/A	493 days (m) 553 days (f)	2/97 (2%)	6/77 (8%)		
			Day 1	i.p.	0.8 mg/g body weight	1×	285 days (m) 343 days (f)	4/30 (13%)[c]	22/39 (56%)[g]		
			8–10 weeks	i.p.	1 mg/g body weight	1×	- 453 days (f)	0/25 (25%)[c]	4/32 (13%)[c]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Urethane (continued)	Mice (Swiss)	leukemia	Control	Control	None	N/A	8–10 months	1%		Highest tumor rates when dosed at birth. Exposure to newborns was followed by 21.6% leukemia, occurring at a mean age of 105 days.	Fiore-Donati et al. (1962)
			Day 1	s.c.	2 mg in 0.05 mL aqueous solution	1×		13/60 (22%)[b]			
			Day 5		4 mg in 0.05 mL aqueous solution	1×		7/39 (18%)[b]			
			Day 40		20 mg in 0.1 mL aqueous solution	1×		2/63 (3%)[b]			
	Mice (Swiss)	lung adenoma	Control 2 weeks	Control	None	N/A	9 weeks	0/15 (0%)	—	The proportion of animals with adenomas decreased steadily with age of exposure.	Rogers (1951)
			Control 4 weeks	Control	None	N/A	11 weeks	0/14 (0%)	—		
			Control 6 weeks	Control	None	N/A	13 weeks	1/15 (7%)	—		
			Control 8 weeks	Control	None	N/A	15 weeks	2/15 (13%)	—		
			Control 10 weeks	Control	None	N/A	17 weeks	0/15 (0%)	—		
			2 weeks	i.p.	1 mg/g body weight	1×	9 weeks	24/24 (100%)[b]	—		
			4 weeks	i.p.	1 mg/g body weight	1×	11 weeks	23/25 (92%)[b]	—		
			6 weeks	i.p.	1 mg/g body weight	1×	13 weeks	22/25 (88%)[b]	—		
			8 weeks	i.p.	1 mg/g body weight	1×	15 weeks	21/25 (84%)[b]	—		
			10 weeks	i.p.	1 mg/g body weight	1×	17 weeks	19/25 (76%)[b]	—		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Urethane (continued)	Mice (Swiss)	lung adenoma	3 weeks	i.p.	0.25 mg/g body weight	1×	12 weeks	16/19 (84%)[b]	—		
					0.5 mg/g body weight	1×	12 weeks	16/20 (80%)[b]	—		
					1 mg/g body weight	1×	12 weeks	18/20 (90%)[b]	—		
			8 weeks	i.p.	0.25 mg/g body weight	1×	17 weeks	4/17 (24%)[b]	—		
					0.5 mg/g body weight	1×	17 weeks	15/16 (94%)[b]	—		
					1 mg/g body weight	1×	17 weeks	18/18 (100%)[b]	—		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
Urethane (continued)	Mice (Swiss)	liver	Control	Control	N/A	N/A	360–720 days	10/227 (4.4%)	4/222 (8.22%)		Chieco-Bianchi et al. (1963)
			Day 1	s.c.	1 mg/g body weight	1×	180 days	1/20 (5%)[g]	0/20 (0%)[c]		
			Day 1	s.c.	1 mg/g body weight	1×	240 days	2/17 (12%)[g]	0/12 (0%)[c]		
			Day 1	s.c.	1 mg/g body weight	1×	300 days	5/18 (28%)[g]	0/16 (0%)[c]		
			Day 1	s.c.	1 mg/g body weight	1×	360 days	11/20 (55%)[g]	0/23 (0%)[c]		
			Day 1	s.c.	1 mg/g body weight	1×	420 days	13/15 (87%)[g]	2/22 (9%)[g]		
			Day 1	s.c.	1 mg/g body weight	1×	480 days	17/23 (74%)[c]	2/25 (8%)[c]		
			Day 5	s.c.	1 mg/g body weight	1×	420 days	9/13 (69.2%)[b]	2/11 (18.2%)[b]		
			Day 20	s.c.	1 mg/g body weight	1×	420 days	1/13 (8%)[b]	0/16 (0%)[b]		
			Day 40	s.c.	1 mg/g body weight	1×	420 days	0/11 (0%)[b]	0/9 (0%)[b]		
	Mice (Swiss)	skin	Control	Control	N/A	N/A	180–550 days	30/712 (4.21%)		Croton oil treatment initiated at 40 days of age.	Chieco-Bianchi et al. (1963)
			Day 1	s.c.	1 mg urethane/g body weight; 5% croton oil	single dose urethane, croton oil applied 2×/week for 10 mos	660 days	26/59 (44.1%)[g]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
Urethane (continued)			Day 40	s.c.	1 mg urethane/g body weight; 5% croton oil	single dose urethane, croton oil applied 2×/week for 10 mos	700 days	8/41 (19.5%)[b]			
	Mice ($B6AF_1/J$)	liver	Control	gavage	N/A	N/A	71 weeks	1/25 (4%)	0/25 (0%)		Klein (1966)
			Day 1		1 mg/g body weight	1×	66 weeks	9/20 (45%)[g]	9/26 (35%)[g]		
			Day 7		1 mg/g body weight	1×	67 weeks	20/22 (91%)[g]	20/26 (77%)[g]		
			Day 14		1 mg/g body weight	1×	68 weeks	16/20 (80%)[g]	10/23 (43%)[g]		
			Day 21		1 mg/g body weight	1×	69 weeks	13/23 (57%)[g]	1/20 (5%)[g]		
			Day 28		1 mg/g body weight	1×	70 weeks	4/24 (17%)[g]	1/20 (5%)[g]		
		lung	Control	gavage	1 mg/g body weight	1×	71 weeks	9/25 (36%)	6/25 (24%)		
			Day 1		1 mg/g body weight	1×	66 weeks	20/20 (100%)[b]	25/26 (96%)[b]		
			Day 7		1 mg/g body weight	1×	67 weeks	22/22 (100%)[b]	26/26 (100%)[b]		
			Day 14		1 mg/g body weight	1×	68 weeks	19/20 (95%)[b]	19/23 (83%)[b]		
			Day 21		1 mg/g body weight	1×	69 weeks	23/23 (100%)[b]	19/20 (95%)[b]		
			Day 28		1 mg/g body weight	1×	70 weeks	24/24 (100%)[b]	20/20 (100%)[b]		
	Mice ($B6AF_1/J$)	Harderian gland	Control	gavage	1 mg/g body weight	1×	71 weeks	0/25 (0%)	0/25 (0%)		Klein (1966)
			Day 1		1 mg/g body weight	1×	66 weeks	0/20 (0%)[c]	1/26 (4%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
Urethane (continued)			Day 7		1 mg/g body weight	1×	67 weeks	0/22 (0%)[c]	1/26 (4%)[b]		
			Day 14		1 mg/g body weight	1×	68 weeks	0/20 (0%)[c]	2/23 (9%)[b]		
			Day 21		1 mg/g body weight	1×	69 weeks	1/23 (4%)[b]	0/20 (0%)[c]		
			Day 28		1 mg/g body weight	1×	70 weeks	0/24 (0%)[c]	0/20 (0%)[c]		
		forestomach	Control	gavage	1 mg/g body weight	1×	71 weeks	0/25 (0%)	1/25 (4%)		
			Day 1		1 mg/g body weight	1×	66 weeks	0/20 (0%)[c]	3/26 (12%)[b]		
			Day 7		1 mg/g body weight	1×	67 weeks	1/22 (5%)[b]	1/26 (4%)[b]		
			Day 14		1 mg/g body weight	1×	68 weeks	1/20 (5%)[b]	4/23 (17%)[b]		
			Day 21		1 mg/g body weight	1×	69 weeks	0/23 (0%)[c]	1/20 (5%)[b]		
			Day 28		1 mg/g body weight	1×	70 weeks	2/24 (8%)[b]	1/20 (5%)[b]		

[a] Where not delineated by gender, data combined by study authors or gender not specified. Where percentages only are given, number of subjects not specified.
[b] Not evaluated by authors.
[c] Evaluated but not significant compared with controls.
[d] Study also included mammary fibroadenomas and fibromas as well as other types of cancers.
[e] 8–9 weeks old.
[f] Includes survivors up to 40 weeks only.
[g] Significant compared with controls.

i.p. = intraperitoneal injection; s.c. = subcutaneous injection

Table 4. Ratio of early-life to adult cancer potencies for studies with repeated exposures of juvenile and adult animals to carcinogens with a mutagenic mode of action*

Compound	Species (strain)	Sex	Dose	Tumor	Unweighted geometric mean	2.5%	Median	97.5%	Reference
Benzidine	Mice ($B6C3F_1$)	male		liver	111	64	**110**	198	Vesselinovitch et al. (1975b)
		female		liver	0.16	0.004	**0.22**	1.1	
3-MU 3-Methylcholanthrene (formerly known as 20-methylcholanthrene)	Mice (Albino)	male	0.25 mg/g	hepatoma	33	7.4	**30**	268	Klein (1959)
		female	0.25 mg/g	hepatoma	7.7	1.1	**7.1**	85	
		male	0.25 mg/g	forestomach	0.91	0.39	**0.91**	2.1	
		female	0.25 mg/g	forestomach	1.5	0.58	**1.5**	4.2	
		male	0.25 mg/g	skin	1.8	0.048	**2.1**	22	
		female	0.25 mg/g	skin	1.5	0.023	**1.8**	21	
Safrole	Mice ($B6C3F_1$)	male		liver	47	16	**44**	198	Vesselinovitch et al. (1979b)
		female		liver	0.12	0.002	**0.18**	1.1	
VC Vinyl chloride	Rats (Sprague-Dawley)	male	6,000 ppm	liver-angiosarcoma	6.7	0.035	**9.8**	57	Maltoni et al. (1984)
		male	10,000 ppm	liver-angiosarcoma	7.4	0.035	**11**	62	
		female	6,000 ppm	liver-angiosarcoma	13	4.9	**13**	33	
		female	10,000 ppm	liver-angiosarcoma	30	8.7	**29**	121	
		male	6,000 ppm	zymbal gland	0.73	0.0032	**1.1**	30	
		male	10,000 ppm	zymbal gland	0.27	0.0022	**0.4**	5.4	
		female	6,000 ppm	zymbal gland	0.48	0.0027	**0.7**	16	
		female	10,000 ppm	zymbal gland	0.15	0.0014	**0.19**	4.5	
		male	10,000 ppm	leukemia	21	0.026	**37**	514	
		female	6,000 ppm	leukemia	1.3	0.0035	**1.7**	153	
		female	10,000 ppm	leukemia	0.29	0.0019	**0.35**	17	
		male	6,000 ppm	nephroblastomas	0.15	0.0014	**0.19**	4.8	
		male	10,000 ppm	nephroblastomas	0.17	0.0015	**0.21**	6.2	
		female	6,000 ppm	nephroblastomas	0.28	0.0018	**0.33**	16	
		female	10,000 ppm	nephroblastomas	0.24	0.0017	**0.29**	11	
		male	6,000 ppm	angiosarcomas-other sites	0.9	0.0033	**1.26**	53	
		male	10,000 ppm	angiosarcomas-	0.25	0.0017	**0.30**	12	

Table 4. Ratio of early-life to adult cancer potencies for studies with repeated exposures of juvenile and adult animals to mutagenic chemicals (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Unweighted geometric mean	2.5%	Median	97.5%	Reference
				other sites					
VC Vinyl chloride (continued)		female	6,000 ppm	angiosarcomas-other sites	0.24	0.0017	**0.29**	11	
		female	10,000 ppm	angiosarcomas-other sites	0.32	0.0019	**0.38**	20	
		male	6,000 ppm	angiomas & fibromas-other sites	0.72	0.0031	**1.0**	33	
		male	10,000 ppm	angiomas & fibromas-other sites	1.4	0.0045	**2.36**	47	
		female	6,000 ppm	angiomas & fibromas-other sites	0.27	0.0018	**0.33**	16	
		female	10,000 ppm	angiomas & fibromas-other sites	0.52	0.0024	**0.63**	41	
		male	6,000 ppm	hepatoma	62	11	**58**	543	
		male	10,000 ppm	hepatoma	34	8.2	**32**	218	
		female	6,000 ppm	hepatoma	55	13	**51**	352	
		female	10,000 ppm	hepatoma	55	8.4	**53**	513	
		male	6,000 ppm	skin carcinomas	1.1	0.0035	**1.5**	82	
		male	10,000 ppm	skin carcinomas	0.41	0.0024	**0.56**	15	
		female	6,000 ppm	skin carcinomas	0.46	0.0024	**0.59**	24	
		female	10,000 ppm	skin carcinomas	0.31	0.0019	**0.37**	19	
		male	6,000 ppm	neuroblastoma	0.21	0.0016	**0.26**	9.5	
		male	10,000 ppm	neuroblastoma	0.20	0.0016	**0.24**	8.5	
		female	6,000 ppm	neuroblastoma	0.27	0.0018	**0.32**	15	
		female	10,000 ppm	neuroblastoma	0.14	0.0014	**0.18**	4.4	

* The 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses.

Table 5. Ratio of early-life to adult cancer potencies for studies with repeated exposures of juvenile and adult animals to chemicals with a nonmutagenic mode of action*

Compound	Species (strain)	Sex	Dose	Tumor	Ratio of juvenile to adult potency				Reference
					Unweighted geometric mean	2.5%	Median	97.5%	
Amitrole	Mice ($B6C3F_1$)	male	NA	liver	13	5.1	**14**	30	Vesselinovitch (1983)
		female	NA	liver	0.14	0.0013	**0.18**	3.9	
DDT	Mice ($B6C3F_1$)	male	NA	liver	1.3	0.0044	**2.5**	25	Vesselinovitch et al. (1979a)
Dieldrin	Mice ($B6C3F_1$)	male	NA	liver	0.75	0.0031	**1.2**	27	Vesselinovitch et al. (1979a)
DPH	Rats (F344/N)	male	630	liver	0.4	0.0024	**0.54**	16	Chhabra et al. (1993b)
		female	630	liver	0.24	0.0017	**0.29**	12	
	Mice ($B6C3F_1$)	male	210	liver	1.5	0.0040	**2.4**	71	
		female	210	liver	1.3	0.0056	**2.6**	15	
ETU	Rats (F344/N)	male	90	thyroid	0.37	0.0029	**0.61**	5.4	Chhabra et al. (1992)
		female	90	thyroid	0.23	0.0018	**0.3**	7.0	
	Mice ($B6C3F_1$)	male	330	liver	0.091	0.0011	**0.12**	1.9	
		female	330	liver	0.057	0.0010	**0.081**	0.65	
		male	330	thyroid	0.41	0.0022	**0.52**	25	
		female	330	thyroid	0.4	0.0024	**0.55**	16	
		male	330	pituitary	0.32	0.0019	**0.38**	22	
		female	330	pituitary	0.24	0.0018	**0.32**	6.9	
PBB	Rats (F344/N)	male	10	liver	0.59	0.0041	**1.1**	6.6	Chhabra et al. (1993a)
		female	10	liver	0.063	0.0009	**0.079**	1.2	
		male	10	mononuclear cell leukemia	0.79	0.0035	**1.4**	18	
		female	10	mononuclear cell leukemia	0.21	0.0017	**0.28**	6.0	
	Mice ($B6C3F_1$)	male	30	liver	3.9	1.9	**3.9**	7.5	
		female	30	liver	1.0	0.37	**1.05**	2.1	

* The 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses.

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action*

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
BaP*	Mice ($B6C3F_1$)	male	75 µg/kg	liver	1 day	9.3	2.9	**8.4**	55	Vesselinovitch et al. (1975a)
					15 days	11	3.5	**9.6**	61	
		female	75 µg/kg		1 day	1.2	0.0083	**1.6**	31	
					15 days	1.7	0.015	**2.1**	36	
		male	150 µg/kg		1 day	29	8.2	**26**	194	
					15 days	15	4.1	**13**	109	
		female	150 µg/kg		1 day	8.8	1.4	**8.1**	94	
					15 days	1.2	0.0082	**1.6**	30	
	Mice ($C3AF_1$)	male	75 µg/kg	liver	1 day	11	2.1	**10**	112	
					15 days	7.5	1.1	**7.0**	83	
		female	75 µg/kg		1 day	0.2	0.0018	**0.26**	9.1	
					15 days	0.2	0.0017	**0.24**	8.5	
		male	150 µg/kg		1 day	14	3.0	**12.8**	130	
					15 days	3.6	0.11	**3.8**	49	
		female	150 µg/kg		1 day	0.2	0.0017	**0.24**	8.8	
					15 days	0.2	0.0017	**0.24**	8.7	
	Mice ($B6C3F_1$)	Male	75 µg/kg	lung	1 day	1.2	0.45	**1.2**	3.4	
					15 days	0.2	0.0046	**0.31**	1.4	
		female	75 µg/kg	lung	1 day	2.8	1.096	**2.7**	9.5	
					15 days	1.4	0.41	**1.4**	5.1	
		Male	150 µg/kg	lung	1 day	2.2	1.0	**2.1**	5.4	
					15 days	0.8	0.2	**0.82**	2.3	
		female	150 µg/kg	lung	1 day	7.9	2.6	**7.2**	43	
					15 days	3.7	1.1	**3.4**	22	
	Mice ($C3AF_1$)	male	75 µg/kg	lung	1 day	1.2	0.47	**1.2**	3.2	
					15 days	1.1	0.43	**1.08**	3.1	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
BaP* (continued)		female	75 µg/kg	lung	1 day	1.6	0.66	**1.55**	4.0	
					15 days	1.6	0.71	**1.63**	4.2	
		male	150 µg/kg	lung	1 day	1.5	0.57	**1.5**	5.0	
					15 days	1.9	0.71	**1.8**	6.0	
		female	150 µg/kg	lung	1 day	1.3	0.61	**1.3**	2.9	
					15 days	1.2	0.54	**1.1**	2.6	
DBA	Mice			lung		178	20	**143**	5100	Law (1940)
DEN**	Mice ($B6C3F_1$)	male	6 µg/kg	liver	1 day	9.0	3.5	**8.3**	37	Vesselinovitch et al. (1984)
					15 days	8.9	3.5	**8.2**	36	
		female	6 µg/kg	liver	1 day	35	9.1	**31**	239	
					15 days	25	6.3	**226**	175	
		male	12 µg/kg	liver	1 day	9.6	3.3	**8.8**	50	
					15 days	9.8	3.4	**8.9**	51	
		female	12 µg/kg	liver	1 day	16	5.9	**15**	67	
					15 days	19	7.1	**18**	79	
	Mice ($C3AF_1$)	male	6 µg/kg	liver	1 day	7.3	2.9	**6.9**	26	
					15 days	3.5	1.4	**3.3**	13	
		female	6 µg/kg	liver	1 day	17	3.2	**16**	166	
					15 days	6.4	0.86	**6.0**	73	
		male	12 µg/kg	liver	1 day	11	3.7	**9.5**	53	
					15 days	9.8	3.4	**8.9**	50	
		female	12 µg/kg	liver	1 day	40	8.5	**36**	340	
					15 days	25	5.0	**22**	221	
	Mice ($B6C3F_1$)	male	6 µg/kg	lung	1 day	0.5	0.27	**0.52**	0.93	
					15 days	1.6	0.95	**1.6**	2.7	
		female	6 µg/kg	lung	1 day	0.9	0.54	**0.89**	1.5	
					15 days	1.2	0.76	**1.2**	2.0	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
DEN** (continued)		male	12 µg/kg	lung	1 day	0.4	0.21	**0.40**	0.73	
					15 days	0.7	0.39	**0.66**	1.1	
		female	12 µg/kg	lung	1 day	0.7	0.44	**0.73**	1.2	
					15 days	1.4	0.88	**1.4**	2.3	
	Mice ($C3AF_1$)	male	6 µg/kg	lung	1 day	0.7	0.22	**0.67**	1.7	
					15 days	0.5	0.21	**0.56**	1.3	
		female	6 µg/kg	lung	1 day	1.1	0.45	**1.1**	2.5	
					15 days	0.7	0.36	**0.74**	1.5	
		male	12 µg/kg	lung	1 day	0.3	0.084	**0.33**	0.76	
					15 days	0.6	0.26	**0.62**	1.4	
		female	12 µg/kg	lung	1 day	0.7	0.35	**0.75**	1.6	
					15 days	0.7	0.37	**0.75**	1.5	
DMBA#	Rats (Wistar)	male		total	2 vs 5–8 wks	3.3	1.3	**3.2**	10	Meranze et al. (1969)
					2 vs 26 wks	3.2	1.3	**3.1**	9.7	
		female		total	2 vs 5–8 wks	1.3	0.68	**1.3**	2.5	
					2 vs 26 wks	3.3	1.2	**3.0**	16	
				mammary	2 vs 5–8 wks	0.0	0.0012	**0.056**	0.26	
					2 vs 26 wks	0.2	0.0023	**0.29**	5.3	
					5 vs 26 wks	7.1	1.8	**6.4**	55	
	Mice (Balb/c)	male	15 µg	lung	1 day	30	2.8	**22**	1482	Walters (1966)
					15–19 days	1.0	0.28	**1.0**	3.5	
		male	30 µgx2	lung	15–19 days	14	1.056	**10**	978	
		female	15 µg	lung	1 day	60	6.0	**46**	2350	
					15–19 days	3.1	0.51	**3.0**	22	
		female	30 µgx2	lung	15–19 days	15	1.2	**11**	1004	
	Mice (Swiss)			lymphoma		2.7	0.60	**2.5**	19	Pietra et al. (1961)
				lung		9.1	2.9	**8.7**	40	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
DMN***	Rats (Wistar)		3 wks	total	1 month	0.7	0.41	**0.73**	1.3	Hard (1979)
					1.5 months	1.1	0.58	**1.1**	2.1	
					2 months	1.5	0.75	**1.5**	3.0	
					3 months	0.9	0.50	**0.94**	1.8	
			24 hr		1 month	0.3	0.13	**0.28**	0.6	
					1.5 months	0.4	0.18	**0.42**	0.9	
					2 months	0.6	0.24	**0.56**	1.3	
					3 months	0.4	0.16	**0.36**	0.78	
			1 month		1.5 months	1.5	0.80	**1.52**	3.0	
					2 months	2.0	1.0	**2.0**	4.2	
					3 months	1.3	0.69	**1.3**	2.5	
ENU	Mice ($B6C3F_1$)	male		liver		7.8	3.9	**7.7**	18	Vesselinovitch (1983)
		female				7.1	2.9	**6.9**	21	
	Rats (Wistar)	male		nerve tissue	1 day	27	2.5	**20**	1374	Naito et al. (1981)
					1 week	1.6	0.61	**1.6**	4.6	
					2 weeks	1.6	0.58	**1.6**	4.8	
					3 weeks	0.7	0.12	**0.72**	2.3	
		female			1 day	64	6.0	**50**	2488	
					1 weeks	9.6	2.6	**8.9**	59	
					2 weeks	6.2	1.6	**5.7**	40	
					3 weeks	0.7	0.0090	**0.89**	8.9	
	Mice ($B6C3F_1$)	male	60 µg/g	lung	1	1.0	0.60	**1.0**	1.7	Vesselinovitch et al. (1974)
					15	1.1	0.66	**1.1**	1.8	
		female	60 µg/g	lung	1	2.1	1.17	**2.1**	4.1	
					15	1.0	0.60	**1.0**	1.7	
		male	120 µg/g	lung	1	1.0	0.60	**1.0**	1.7	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
					15	1.1	0.66	**1.0**	1.8	
ENU (continued)		female	120 µg/g	lung	1	2.1	1.2	**2.1**	4.1	
					15	1.0	0.60	**1.0**	1.7	
	Mice ($C3AF_1$)	male	60 µg/g	lung	1	8.7	2.7	**8.0**	48	
					15	52	5.2	**39**	2141	
		female	60 µg/g	lung	15	0.7	0.32	**0.72**	1.6	
		male	120 µg/g	lung	1	0.9	0.38	**0.92**	2.2	
					15	0.7	0.28	**0.67**	1.6	
		female	120 µg/g	lung	1	0.5	0.24	**0.54**	1.2	
					15	0.4	0.18	**0.42**	0.92	
	Mice ($B6C3F_1$)	male	60 µg/g	liver	1	8.8	4.2	**8.5**	22	
					15	14	6.2	**14**	37	
		female	60 µg/g	liver	1	6.3	2.6	**6.1**	18	
					15	5.6	2.4	**5.4**	16	
		male	120 µg/g	liver	1	5.2	2.5	**5.1**	11	
					15	7.6	3.9	**7.5**	17	
		female	120 µg/g	liver	1	11	4.1	**11**	46	
					15	14	4.9	**13**	55	
	Mice ($C3AF_1$)	male	60 µg/g	liver	1	12	4.7	**11**	43	
					15	8.1	3.2	**7.6**	29	
		female	60 µg/g	liver	1	7.5	2.6	**7.0**	32	
					15	4.8	1.8	**4.6**	18	
		male	120 µg/g	liver	1	9.8	4.1	**9.3**	32	
					15	6.6	2.7	**6.3**	23	
		female	120 µg/g	liver	1	5.4	1.7	**5.0**	25	
					15	5.4	1.7	**5.1**	25	
	Mice ($B6C3F_1$)	male	60 µg/g	kidney	1	2.2	0.73	**2.1**	8.0	
					15	1.2	0.29	**1.2**	5.1	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
		female	60 µg/g	kidney	1	0.7	0.024	**0.85**	5.9	
					15	2.6	0.61	**2.5**	15	
ENU (continued)		male	120 µg/g	kidney	1	1.7	0.65	**1.7**	4.4	
					15	2.6	1.14	**2.6**	6.4	
		female	120 µg/g	kidney	1	0.9	0.37	**0.87**	2.0	
					15	1.4	0.67	**1.4**	3.2	
	Mice ($C3AF_1$)	male	60 µg/g	kidney	1	1.8	0.17	**1.9**	15	
					15	2.0	0.25	**2.0**	16	
		female	60 µg/g	kidney	1	1.0	0.016	**1.3**	13	
					15	2.1	0.16	**2.2**	20	
		male	120 µg/g	kidney	1	0.2	0.0029	**0.24**	1.5	
					15	1.5	0.38	**1.5**	5.9	
		female	120 µg/g	kidney	1	2.3	0.17	**2.4**	20	
					15	7.1	1.8	**6.5**	47	
	Mice ($B6C3F_1$)	male	60 µg/g	Harderian	1	0.3	0.018	**0.41**	1.4	
					15	0.5	0.075	**0.52**	1.4	
		female	60 µg/g	Harderian	1	0.1	0.0025	**0.16**	0.74	
					15	0.8	0.35	**0.84**	2.0	
		male	120 µg/g	Harderian	1	0.4	0.13	**0.42**	0.96	
					15	0.6	0.26	**0.57**	1.2	
		female	120 µg/g	Harderian	1	0.1	0.0030	**0.18**	0.85	
					15	0.7	0.17	**0.77**	2.1	
	Mice ($C3AF_1$)	male	60 µg/g	Harderian	1	0.1	0.0023	**0.20**	1.3	
					15	0.1	0.0016	**0.18**	1.8	
		female	60 µg/g	Harderian	1	0.4	0.019	**0.52**	2.5	
					15	0.8	0.15	**0.85**	3.4	
		male	120 µg/g	Harderian	1	0.1	0.0010	**0.086**	1.0	
					15	0.3	0.0050	**0.40**	2.8	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
		female	120 µg/g	Harderian	1	0.1	0.0012	**0.094**	1.2	
					15	0.1	0.0012	**0.081**	0.90	
ENU (continued)	Mice ($B6C3F_1$)	male	60 µg/g	stomach	1	0.3	0.0091	**0.34**	2.4	
					15	1.9	0.61	**1.82**	8.7	
		female	60 µg/g	stomach	1	0.2	0.0083	**0.26**	1.1	
					15	0.2	0.0072	**0.24**	1.0	
		male	120 µg/g	stomach	1	0.2	0.0059	**0.20**	0.90	
					15	1.2	0.50	**1.2**	2.9	
		female	120 µg/g	stomach	1	0.6	0.19	**0.60**	1.5	
					15	1.6	0.67	**1.6**	3.7	
	Mice ($C3AF_1$)	male	60 µg/g	stomach	1	0.0	0.0009	**0.063**	0.51	
					15	0.3	0.023	**0.41**	1.3	
		female	60 µg/g	stomach	1	0.8	0.085	**0.89**	3.5	
					15	1.1	0.19	**1.1**	4.5	
		male	120 µg/g	stomach	1	0.2	0.010	**0.19**	0.56	
					15	0.7	0.32	**0.70**	1.5	
		female	120 µg/g	stomach	1	0.4	0.14	**0.46**	1.2	
					15	0.6	0.24	**0.64**	1.5	
NMU	Mice ($BC3F_1$)	male	50 µg/g	lung adenomas	1	3.4	1.3	**3.3**	9.3	Terracini and Testa (1970)
		female	50 µg/g	lung adenomas	1	6.3	2.4	**6.0**	23	
		male	50 µg/g	lymphosarcoma	1	2.5	1.1	**2.4**	6.4	
		female	50 µg/g	lymphosarcoma	1	1.1	0.49	**1.1**	2.4	
		male	50 µg/g	hepatoma	1	35	6.5	**32**	324	
		female	50 µg/g	hepatoma	1	0.3	0.0023	**0.39**	13	
		male	50 µg/g	renal adenoma	1	0.9	0.0093	**1.2**	13	
		female	50 µg/g	renal adenoma	1	1.3	0.0081	**1.7**	33	
		male	50 µg/g	forestomach	1	0.0	0.0006	**0.039**	0.52	
		female	50 µg/g	forestomach	1	0.1	0.0027	**0.15**	0.69	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
	Mice (C3Hf/Dp)	male	25 µg/g	thymic lymphoma	1	1.9	0.048	**2.1**	23	
NMU (continued)		female	25 µg/g	thymic lymphoma	1	1.2	0.0089	**1.5**	30	
		male	25 µg/g	lung adenomas	1	1.0	0.013	**1.2**	11	
		female	25 µg/g	lung adenomas	1	0.4	0.018	**0.46**	1. 7	
		male	25 µg/g	liver tumor	1	0.2	0.0016	**0.21**	4.6	
		female	25 µg/g	liver tumor	1	0.3	0.0026	**0.39**	4.4	
		male	25 µg/g	Stomach	1	0.5	0.0045	**0.67**	6.8	
		female	25 µg/g	Stomach	1	0.3	0.0046	**0.43**	3.8	
				ovarian	1	0.1	0.0014	**0.17**	3.5	
				uterine/vaginal	1	8.6	1.1	**8.1**	97	
		male	50 µg/g	thymic lymphoma	1	7.9	3.1	**7.4**	30	
		female	50 µg/g	thymic lymphoma	1	3.1	1.3	**3.0**	7.8	
		male	50 µg/g	lung adenomas	1	0.04	0.0008	**0.058**	0.45	
		female	50 µg/g	lung adenomas	1	0.1	0.0012	**0.084**	0.53	
		male	50 µg/g	liver tumor	1	0.2	0.0021	**0.33**	7.8	
		female	50 µg/g	liver tumor	1	0.1	0.0011	**0.13**	4.5	
		male	50 µg/g	Stomach	1	0.01	0.0003	**0.013**	0.12	
		female	50 µg/g	Stomach	1	0.1	0.0022	**0.15**	0.96	
				ovarian	1	0.0	0.0003	**0.014**	0.14	
				uterine/vaginal	1	0.0	0.0005	**0.034**	0.46	
		male	50 µg/g	thymic lymphoma	21	4.3	1. 6	**4.1**	17	
		female	50 µg/g	thymic lymphoma	21	1.0	0.39	**1.0**	2.6	
		male	50 µg/g	lung adenomas	21	0.1	0.0022	**0.22**	1.1	
		female	50 µg/g	lung adenomas	21	0.7	0.30	**0.75**	1.7	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
		male	50 µg/g	liver tumor	21	0.1	0.0013	**0.15**	4.3	
		female	50 µg/g	liver tumor	21	0.9	0.0051	**1.4**	23	
NMU (continued)		male	50 µg/g	stomach	21	0.1	0.001	**0.08**	0.64	
		female	50 µg/g	stomach	21	1.8	0.77	**1.8**	4.7	
				ovarian	21	0.0	0.0007	**0.055**	0.97	
				uterine/vaginal	21	1.7	0.59	**1.7**	6.4	
Urethane	Mice (Swiss)	male	1 mg/g	liver	1	24	4.4	**21**	220	Chieco-Bianchi et al. (1963)
		female	1 mg/g	liver	1	0.4	0.0044	**0.54**	13	
		male	1 mg/g	liver	5	14	2.4	**13**	137	
		female	1 mg/g	liver	5	1.2	0.017	**1.4**	26	
		male	1 mg/g	liver	20	0.2	0.0018	**0.28**	10	
		female	1 mg/g	liver	20	0.1	0.0011	**0.12**	4.8	
		both	1 mg/g	skin	1	0.2	0.0027	**0.32**	5.4	
Urethane + croton oil	Mice (Swiss)	both	1 mg/g	skin	1	2.9	1.2	**2.8**	8.2	
Urethane	Rats (MRC Wistar-derived)	male/ female	16%×6	neurilemmomas	1	0.2	0.0028	**0.33**	4.5	Choudari Kommineni et al. (1970)
		male/ female	16%×6	neurilemmomas	28	0.4	0.0045	**0.51**	6.3	
		male/ female	16%×6	liver	1	7.9	1.4	**7.1**	82	
		male/ female	16%×6	liver	28	0.2	0.0026	**0.4**	11.7	
		male/ female	16%×6	thyroid	1	0.0	0.0006	**0.039**	0.67	
		male/ female	16%×6	thyroid	28	0.1	0.0011	**0.1**	1.5	
	Mice (Swiss)	male/ female	1 mg/g	lung	1	15	1.2	**11**	997	De Benedictis et al. (1962)
	Mice (Swiss)			leukemia		6.7	1.7	**6.1**	45	Fiore-Donati et al.

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
						5.1	1.1	**4.7**	38	(1962)
Urethane (continued)	Mice ($B6AF_1/J$)	male	1 mg/g	liver	21	5.1	1.4	**4.7**	30	Klein (1966)
		female	1 mg/g	liver	21	0.2	0.0019	**0.26**	6.0	
				Harderian gland	1	0.3	0.0021	**0.33**	11	
					7	0.3	0.0021	**0.33**	11	
					14	0.6	0.0044	**0.85**	20	
		male	1 mg/g	Harderian gland	21	0.3	0.0024	**0.41**	13	
		male	1 mg/g	forestomach	1	0.1	0.0009	**0.079**	1.9	
		female	1 mg/g	forestomach	1	0.4	0.0028	**0.49**	11	
		male	1 mg/g	forestomach	7	0.1	0.0017	**0.19**	3.5	
		female	1 mg/g	forestomach	7	0.1	0.0013	**0.16**	5.0	
		male	1 mg/g	forestomach	14	0.2	0.0018	**0.21**	3.9	
		female	1 mg/g	forestomach	14	0.8	0.0056	**1.1**	18	
		male	1 mg/g	forestomach	21	0.1	0.0008	**0.072**	1.7	
		female	1 mg/g	forestomach	21	0.2	0.0015	**0.2**	6.3	
				lung	1	1.0	0.36	**0.95**	2.5	
		male	1 mg/g	lung	14	0.8	0.26	**0.8**	2.3	
		female	1 mg/g	lung	14	0.4	0.16	**0.45**	1.1	
					21	0.9	0.31	**0.86**	2.4	
	Mice (C3H/f)	male	1 mg/g	liver	1	14	4.0	**12**	81	Liebelt et al. (1964)
		female	1 mg/g	liver	1	16	3.2	**15**	155	
		male	1 mg/g	lung	1	5.9	1.7	**5.6**	28	
		female	1 mg/g	lung	1	22	4.5	**20**	203	
		male	1 mg/g	reticular tissue	1	2.0	0.023	**2.3**	38	
		female	1 mg/g	reticular tissue	1	8.6	2.3	**7.7**	60	
	Mice (Swiss)		1 mg/g	pulmonary adenomas	2 vs 4 weeks	14	1.1	**10.1**	965	Rogers (1951)

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
			1 mg/g	pulmonary adenomas	2 vs 6 weeks	16	1.3	**11.3**	1025	
Urethane (continued)			1 mg/g	pulmonary adenomas	2 vs 8 weeks	19	1.6	**13.3**	1126	
			1 mg/g	pulmonary adenomas	2 vs 10 weeks	21	1.9	**14.5**	1168	
			0.25 mg/g	adenomas	3 vs 8 weeks	7.1	2.3	**6.7**	29	
			0.5 mg/g	adenomas	3 vs 8 weeks	0.7	0.29	**0.67**	1.6	
			1.0 mg/g	adenomas	3 vs 8 weeks	0.7	0.28	**0.68**	1.6	

* The 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses.

Table 7. Ratio of early-life to adult cancer potencies for studies with lifetime exposures starting with juvenile and adult animals to carcinogens with mutagenic or nonmutagenic modes of action*

Compound	Species (strain)	Sex	Dose	Tumor	Unweightedg eometric mean	2.5%	Median	97.5%	Reference
Mutagenic compounds									
DEN	Rats (Colworth)		multiple	liver	2.8	0.0093	**5.6**	23	Peto et al. (1984)
				esophagus	0.18	0.0015	**0.23**	4.8	
Safrole	Mice ($B6C3F_1$)	male		liver	50	3.7	**50**	253	Vesselinovitch et al. (1979b)
		female		liver	4.0	0.007	**4.0**	23	
Urethane	Mice ($B6AF_1/J$)	male	2.5 mg/pup	liver	79	0.36	**102**	1,064	Klein (1966)
		female	2.5 mg/pup	liver	0.47	0.0022	**0.55**	42	
Nonmutagenic compounds									
DDT	Mice ($B6C3F_1$)			liver	23	0.0023	**0.58**	23	Vesselinovitch et al. (1979a)
Dieldrin	Mice ($B6C3F_1$)			liver	91	0.014	**14**	91	Vesselinovitch et al. (1979a)
DPH	Rats (F344/N)	male	630:800	liver	0.31	0.0019	**0.37**	18	Chhabra et al. (1993b)
			630:2,400	liver	0.36	0.0021	**0.45**	17	
		female	630:800	liver	0.33	0.0019	**0.39**	21	
			630:2,400	liver	0.33	0.0019	**0.39**	21	
	Mice ($B6C3F_1$)	male	210:100	liver	0.71	0.0028	**0.93**	49	
			210:300	liver	14	0.03	**23**	214	
		female	210:200	liver	0.32	0.002	**0.42**	13	
			210:600	liver	0.35	0.0023	**0.53**	8.8	
ETU	Rats (F344/N)	male	90:83	thyroid	0.23	0.0017	**0.3**	7.3	Chhabra et al. (1992)
			90:250	thyroid	9.1	1.1	**10.5**	27	
		female	90:83	thyroid	0.37	0.0021	**0.46**	19	
			90:250	thyroid	0.61	0.0034	**1.1**	10	

Table 7. Ratio of early-life to adult cancer potencies for studies with lifetime exposures starting with juvenile and adult animals to carcinogens with mutagenic or nonmutagenic modes of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Unweighted geometric mean	2.5%	Median	97.5%	Reference
ETU (continued)	Mice ($B6C3F_1$)	male	330:330	liver	0.37	0.0022	**0.5**	14	
			330:1,000	liver	0.48	0.0027	**0.75**	12	
		female	330:330	liver	0.33	0.0023	**0.5**	7.8	
			330:1,000	liver	0.42	0.0025	**0.65**	11	
		male	330:330	thyroid	0.44	0.0022	**0.52**	34	
			330:1,000	thyroid	0.63	0.0035	**1.12**	10	
		female	330:330	thyroid	5.2	0.011	**10**	108	
			330:1,000	thyroid	0.18	0.0016	**0.24**	4.2	
		male	330:330	pituitary	0.40	0.0021	**0.47**	32	
			330:1,000	pituitary	0.18	0.0015	**0.22**	5.7	
		female	330:330	pituitary	0.21	0.0016	**0.26**	10	
			330:1,000	pituitary	0.27	0.0019	**0.36**	9.0	
PBB	Rats (F344/N)	male	10:10	liver	0.39	0.0023	**0.56**	13	Chhabra et al. (1993a)
			10:30	liver	0.18	0.0016	**0.25**	4.3	
		female	10:10	liver	36	15	**36**	86	
			10:30	liver	3.1	0.023	**4.6**	22	
		male	10:10	mononuclear cell leukemia	0.51	0.0025	**0.69**	23	
		male	10:30	mononuclear cell leukemia	0.77	0.0031	**1.1**	35	
		female	10:10	mononuclear cell leukemia	0.54	0.0026	**0.74**	24	
		female	10:30	mononuclear cell leukemia	0.34	0.0021	**0.45**	15	
	Mice ($B6C3F_1$)	male	30:30	liver	8.9	0.015	**12.2**	1,076	
		female	30:30	liver	4.4	0.0075	**6.2**	786	
		male	10:10	liver	0.15	0.0014	**0.2**	3.9	

Table 7. Ratio of early-life to adult cancer potencies for studies with lifetime exposures starting with juvenile and adult animals to carcinogens with mutagenic or nonmutagenic modes of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Unweighted geometric mean	2.5%	Median	97.5%	Reference
		female	10:10	liver	0.29	0.0021	**0.43**	7.0	

* The 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses.

Table 8. Summary of quantitative estimates of ratio of early-life to adult cancer potencies

Dose	Tissue	Number of chemicals	Inverse-weighted geometric mean ratio	Unweighted Minimum	Unweighted Maximum	Number of ratios	Percentage >1
Chemicals with mutagenic mode of action							
Repeated		4	10.5	0.12	111	45	42
Lifetime		3	8.7	0.18	79	6	67
	Combined repeated and lifetime	**6**	**10.4**	**0.12**	**111**	**51**	**45**
Acute	**Combined**	11	1.5	0.01	178	268	55
	Forestomach	3	0.076	0.01	1.9	32	16
	Harderian	2	0.48	0.06	0.8	20	0.0
	Kidney	2	1.6	0.17	7.1	18	78
	Leukemia	1	5.9	5.1	6.7	2	100
	Liver	5	8.1	0.10	40	70	77
	Lung	7	1.1	0.04	178	77	56
	Lymph	2	1.8	1.1	2.7	3	100
	Mammary (wk 5 vs wk 26)	1	7.1	NA	NA	1	100
	Mammary (wk 2 vs wk 5–8 or 26)	1	0.071	NA	NA	2	0
	Nerve	2	2.3	0.24	64	8	75
	Nerve (Day 1 comparison)	2	10	0.24	64	3	67
	Ovarian	1	0.033	0.01	0.13	3	0
	Reticular tissue	1	6.5	1.96	8.6	2	100
	Thymic lymphoma	1	2.8	1.01	7.9	6	100
	Thyroid	1	0.05	0.03	0.08	2	0
	Uterine/vaginal	1	1.6	0.03	8.6	3	67
	Day 1	7	1.7	0.01	178	127	55
	Day 15	3	1.5	0.06	52	74	65
Chemicals with nonmutagenic mode of action							
Repeated		6	2.2	0.06	13	22	27
Lifetime		5	3.4	0.15	36	38	21

Table 9. Excess Relative Risk (ERR) estimates for cancer incidence from Life Span Study (Japanese survivors)[a]

Site	Average ERR at 1 Sv	
	<20[b]	>20[b]
Stomach	0.74	0.24
Colon	0.62	0.7
Liver	1.3	0.31
Lung	0.57	1.1
Bone and connective tissue	11	0.42
Skin	5.4	0.39
Breast	3.3	0.98
Urinary bladder	0.71	0.79
Leukemia	6.1	3.7

[a] Information extracted from tables in UNSCEAR, Annex I (2000).
[b] Age at exposure.

Table 10. Excess Relative Risk (ERR) estimates for incidence of thyroid cancer from Life Span Study[a]

Age at exposure	Average ERR at 1 Sv (No. cases)
0–9 yr	10.25 (24)
10–19 yr	4.5 (35)
20–29 yr	0.10 (18)
>30 yr	0.04 (55)

[a] Information extracted from tables in UNSCEAR, Annex I (2000).

Table 11. Coefficients for the Revised Methodology mortality risk model (from U.S. EPA, 1999)[a]

Cancer type	Risk model type[b]	Age group				
		0–9	10–19	20–29	30–39	40+
Male:						
Stomach	R	1.223	1.972	2.044	0.3024	0.2745
Colon	R	2.290	2.290	0.2787	0.4395	0.08881
Liver	R	0.9877	0.9877	0.9877	0.9877	0.9877
Lung	R	0.4480	0.4480	0.0435	0.1315	0.1680
Bone	A	0.09387	0.09387	0.09387	0.09387	0.09387
Skin	A	0.06597	0.06597	0.06597	0.06597	0.06597
Breast	R	0.0	0.0	0.0	0.0	0.0
Ovary	R	0.0	0.0	0.0	0.0	0.0
Bladder	R	1.037	1.037	1.037	1.037	1.037
Kidney	R	0.2938	0.2938	0.2938	0.2938	0.2938
Thyroid	A	0.1667	0.1667	0.1667	0.1667	0.1667
Leukemia	R	982.3	311.3	416.6	264.4	143.6
Female:						
Stomach	R	3.581	4.585	4.552	0.6309	0.5424
Colon	R	3.265	3.265	0.6183	0.8921	0.1921
Liver	R	0.9877	0.9877	0.9877	0.9877	0.9877
Lung	R	1.359	1.359	0.1620	0.4396	0.6047
Bone	A	0.09387	0.09387	0.09387	0.09387	0.09387
Skin	A	0.06597	0.06597	0.06597	0.06597	0.06597
Breast	R	0.7000	0.7000	0.3000	0.3000	0.1000
Ovary	R	0.7185	0.7185	0.7185	0.7185	0.7185
Bladder	R	1.049	1.049	1.049	1.049	1.049
Kidney	R	0.2938	0.2938	0.2938	0.2938	0.2938
Thyroid	A	0.3333	0.3333	0.1667	0.1667	0.1667
Leukemia	R	1,176	284.9	370.06	178.8	157.1

[a] The coefficients were derived using several models applied to data from A-bomb survivors and selected medical exposures.

[b] A = absolute risk with coefficient units of 10^{-4} $(Gy\ y)^{-1}$; R= relative risk with coefficient units of Gy^{-1}.

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Exhibit E

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Risk Assessment Guidance for Superfund
Volume I: Human Health Evaluation Manual
(Part F, Supplemental Guidance for Inhalation Risk Assessment)

Final

Office of Superfund Remediation and Technology Innovation
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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF EQUATIONS

LIST OF EQUATIONS (CONT.)

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Marcia Bailey, Region 10
Bob Benson, Region 8
Dave Crawford, OSWER/OSRTI
Arunas Draugelis, Region 5
Brenda Foos, OCHP
Gary Foureman, ORD/NCEA
Susan Griffin, Region 8
Ofia Hodoh, Region 4
Jennifer Hubbard, Region 3
Ann Johnson, OA/OPEI
Jeremy Johnson, Region 7
Kevin Koporec, Region 4
Sarah Levinson, Region 1
Deirdre Murphy, OAR/OAQPS
Henry Schuver, OSWER/OSW
Michael Sivak, Region 2
John Stanek, ORD/NCEA
Daniel Stralka, Region 9
Timothy Taylor, OSWER/OSW
John Whalan, ORD/NCEA
Erik Winchester, ORD/OSP

Former Members:
Cheryl Overstreet, Region 6
Neil Stiber, ORD/OSP

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Sandra Baird, Massachusetts Department of Environmental Protection
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LIST OF ACRONYMS

µg	Microgram
µm	Micrometer
ADAF	Age Dependent Adjustment Factor
AT	Averaging Time
ATSDR	Agency for Toxic Substances and Disease Registry
BMCL	Benchmark Concentration, Lower confidence limit
BMD	Benchmark Dose
BW	Body Weight
CA	Contaminant Concentration in Air
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CSF	Cancer Slope Factor
DAF	Dosimetric Adjustment Factor
ED	Exposure Duration
EC	Exposure Concentration
EF	Exposure Frequency
EPA	Environmental Protection Agency
ER	Extra-respiratory
ET	Exposure Time
ETh	Extrathoracic
F_r	Fractional Deposition in region r
F_{total}	Total particle deposition in respiratory tract
$H_{b/g\text{-}animal}$	Animal Blood:Gas Partition Coefficient
$H_{b/g\text{-}human}$	Human Blood:Gas Partition Coefficient
HEAST	Health Effects Assessment Summary Table
HEC	Human Equivalent Concentration
HI	Hazard Index
HQ	Hazard Quotient
ICRP	International Commission for Radiological Protection
IR	Inhalation Rate
IRIS	Integrated Risk Information System
IUR	Inhalation Unit Risk
kg	Kilogram
LEC_{10}	Lower limit on Effective Concentration, using a 10 percent response level
LOAEL	Lowest Observable Adverse Effect Level
ME	Microenvironment
MF	Modifying Factor
mg	Milligram
MOA	Mode of Action
MRL	Minimal Risk Level
MW	Molecular Weight
NCEA	National Center for Environmental Assessment
NOAEL	No Observable Adverse Effect Level
ORD	Office of Research and Development
OSRTI	Office of Superfund Remediation and Technology Innovation

LIST OF ACRONYMS (CONT.)

OSWER	Office of Solid Waste and Emergency Response
PBPK	Physiologically Based Pharmacokinetic
POD	Point of Departure
ppm	Parts Per Million
PPRTV	Provisional Peer Reviewed Toxicity Value
PRG	Preliminary Remediation Goal
PU	Pulmonary
Q-alv	Alveolar ventilation rate
QSAR	Quantitative Structure-Activity Relationship
RAGS	Risk Assessment Guidance for Superfund
RBC	Risk-Based Concentration
RfC	Reference Concentration
RfD	Reference Dose
RGDR	Regional Gas Dose Ratio
RDDR	Regional Deposited Dose Ratio
RME	Reasonable Maximum Exposure
SA	Surface Area
SSL	Soil Screening Level
STSC	Superfund Health Risk Technical Support Center
TB	Tracheobronchial
TOT	Total Respiratory System
UF	Uncertainty Factor
V_e	Minute Volume

1. INTRODUCTION

The Environmental Protection Agency's (EPA's) Superfund Program has updated its approach for determining risk from inhaled chemicals to be consistent with the inhalation dosimetry methodology described in *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994; hereafter, the *Inhalation Dosimetry Methodology*).[1] This document provides Superfund site risk assessors with guidance that should help more consistently address the *Inhalation Dosimetry Methodology*.

This document outlines recommended processes consisting of a series of steps as well as recommended equations for EPA Regions to consider when estimating inhalation exposure and risk at Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) sites. This guidance is intended to provide a recommended methodology for consistently addressing the inhalation pathway in risk assessments for Superfund sites.

Some of the statutory provisions described in this document contain legally binding requirements. However, this document does not substitute for those provisions or regulations, nor is it a regulation itself. Thus, it cannot impose legally binding requirements on EPA, States, or the regulated community, and may not apply to a particular situation based upon the circumstances. Any decisions regarding a particular remedy selection decision will be made based on the statute and regulations, and EPA decisionmakers retain the discretion to adopt approaches on a case-by-case basis that differ from this guidance where appropriate. EPA may change this guidance in the future.

1.1 Background

EPA's *Risk Assessment Guidance for Superfund (RAGS), Part A* (USEPA, 1989; hereafter, *RAGS, Part A*) outlined a previously recommended approach for conducting site-specific baseline risk assessments for inhaled contaminants.[2] According to the original RAGS approach, the inhalation exposure estimate was typically derived in terms of a chronic, daily "air intake" (mg/kg-day) using the following general approach. The intake of the chemical was estimated as a function of the concentration of the chemical in air (CA), inhalation rate (IR), body weight (BW), and the exposure scenario. Age-specific values for BW and IR were used when evaluating childhood exposures. Table 1 presents the *RAGS, Part A* equation for calculating intake for inhalation exposure. Inhalation toxicity values were "converted" into similar units for the risk quantification step. Cancer risk was estimated by multiplying the chronic daily intake of the chemical from the air by the "inhalation cancer slope factor" (CSF_i); the Hazard Quotient (HQ) for non-cancer effects was estimated by dividing the intake of the chemical by an "inhalation reference dose" (RfD_i).[3]

The approach outlined in *RAGS, Part A* was developed before EPA issued the *Inhalation Dosimetry Methodology*, which describes the Agency's refined recommended approach for interpreting

[1] The *Inhalation Dosimetry Methodology* can be found at the following web address: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=71993.

[2] See sections 6.6.3, 7.2.3, 7.3.3, and 8.2 of *RAGS, Part A*.

[3] EPA defines an HQ in *RAGS, Part A* as: "The ratio of a single substance exposure level over a specified time period (e.g., subchronic) to a reference dose (RfD) for that substance derived from a similar exposure period" (USEPA, 1989).

inhalation toxicity studies in laboratory animals or studies of occupational exposures of humans to airborne chemicals. Under the *Inhalation Dosimetry Methodology*, the experimental exposures are typically extrapolated to a Human Equivalent Concentration (HEC), and a reference concentration (RfC) is typically calculated by dividing the HEC by uncertainty factors (UFs). As described in the Agency's *Guidelines for Cancer Risk Assessment* (USEPA, 2005a), the HEC developed in accordance with the *Inhalation Dosimetry Methodology* typically is also used in developing an inhalation unit risk (IUR) for cancer risk assessment (which may also be called an inhalation cancer slope factor).[4] The procedure that was used to calculate the published RfC or IUR is described in the Integrated Risk Information System (IRIS) profile or other toxicological reference document for a chemical.

TABLE 1
RAGS, PART A EQUATION DESCRIBING THE ESTIMATION OF INHALATION EXPOSURE

Equation	Location in RAGS, Part A
Intake (mg/kg-d) = CA x (IR/BW) x (ET x EF x ED)/AT	Exhibit 6-16, Page 6-44
Key: CA (mg/m^3) = contaminant concentration in air; IR (m^3/hr) = inhalation rate; BW (kg) = body weight; ET (hours/day) = exposure time; EF (days/year) = exposure frequency; ED (years) = exposure duration; and AT (days) = averaging time (period over which exposure is averaged).	

The Superfund Program has updated its inhalation risk paradigm to be compatible with the *Inhalation Dosimetry Methodology*, which represents the Agency's current methodology for inhalation dosimetry and derivation of inhalation toxicity values.[5] This document recommends that when estimating risk via inhalation, risk assessors should use the concentration of the chemical in air as the exposure metric (e.g., mg/m^3), rather than inhalation intake of a contaminant in air based on IR and BW (e.g., mg/kg-day).

1.2 Purpose and Scope

The intake equation described above (*RAGS, Part A*, Exhibit 6-16) is not consistent with the principles of EPA's *Inhalation Dosimetry Methodology* because the amount of the chemical that reaches the target site is not a simple function of IR and BW. Instead, the interaction of the inhaled contaminant with the respiratory tract is affected by factors such as species-specific relationships of exposure concentrations (ECs) to deposited/delivered doses and physiochemical characteristics of the inhaled contaminant. The *Inhalation Dosimetry Methodology* also considers the target site where the toxic effect occurs (e.g., the respiratory tract or a location in the body remote from the portal-of-entry) when applying dosimetric adjustments to experimental concentrations (USEPA, 1994). Therefore, this *RAGS, Part A* equation is not recommended for estimating exposures to inhaled contaminants.

[4] The phrase "inhalation cancer slope factor," as used in this guidance, refers generally to the risk per a measure of inhalation exposure. Inhalation exposure in cancer bioassays or occupational studies from which slope factors may be derived is most commonly expressed as an exposure concentration (e.g., µg agent/m^3 air). Please note that this differs from past use of the phrase "inhalation cancer slope factor" or "CSF_i" by the Superfund program to refer to a cancer slope expressed as an "inhalation intake" (e.g., *RAGS, Part A* (USEPA, 1989)).

[5] For additional information about the Superfund program's adoption of the *Inhalation Dosimetry Methodology*, please refer to the summary of a 2003 Superfund workshop on inhalation risk assessment: http://www.epa.gov/oswer/riskassessment/pdf/finalinhalationriskworkshop.pdf.

The purpose of this document is to provide a recommended approach for developing the information necessary to assist risk assessment and risk management decision-making at waste sites involving potential risks from inhalation exposures.[6, 7] This includes providing equations that may be used in conducting baseline risk assessments and in calculating risk-based concentrations (RBCs). It is intended that *RAGS, Part F* will replace those portions of *RAGS, Part A*, which addressed inhalation risk.

1.3 Effects on Other Office of Superfund Remediation and Technology Innovation Guidance

EPA recommends that the intake equation presented in *RAGS, Part A* (USEPA, 1989, Exhibit 6-16) should no longer be used when evaluating risk from the inhalation pathway. Implementation of a risk assessment approach consistent with the *Inhalation Dosimetry Methodology* will also affect the following guidance documents: *RAGS, Part B*, Section 3.3: Volatilization and Particulate Emission Factors (USEPA, 1991); and the Office of Solid Waste and Emergency Response's (OSWER's) *Draft Guidance for Evaluating the Vapor Intrusion to Indoor Air Pathway from Groundwater and Soils* (USEPA, 2002a; hereafter the *Vapor Intrusion Guidance*). EPA no longer recommends using the equations in Section 3.3 of *RAGS, Part B* nor the inhalation toxicity values generated using simple route-to-route extrapolation, such as those presented in the 2002 draft *Vapor Intrusion Guidance* and related documents.[8]

This guidance does not affect the equations pertaining to risk from inhaled chemicals in the *Soil Screening Guidance* (USEPA, 1996), Section 2.4, or the *Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites* (USEPA, 2002b), Sections 4.2.3, 5.3.2 and Appendix B, other than to clarify that the IURs and RfCs used in the equations are based on continuous exposure (24 hours per day). If the exposure scenario of interest is less than 24 hours per day, the scenario-specific exposure time (ET) in hours per day should be used in the equations and the averaging time should be in units of hours (see Equations 6 and 8 in this document). *RAGS, Part D* (USEPA, 2001) is also not affected by *RAGS, Part F*, as it includes sufficient flexibility to accommodate the revisions described in this guidance. In addition, the screening values presented on the "Regional Screening Levels for Chemical Contaminants at Superfund Sites" screening level/preliminary remediation goal table are consistent with *RAGS, Part F* (USEPA, 2008a).[9] Readers can contact EPA headquarters with questions about the compatibility of specific Superfund documents with *RAGS, Part F*.

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[6] Note that the assessment of risk from inhaled nanoparticles is outside the scope of this document.

[7] If a site contains asbestos contamination, risk assessors should contact EPA's Technical Review Workgroup for Metals and Asbestos for assistance.

[8] Related documents include the *Johnson and Ettinger (1991) Model for Subsurface Vapor Intrusion into Buildings* spreadsheet models (http://www.epa.gov/oswer/riskassessment/airmodel/johnson_ettinger.htm) and the accompanying *User's Guide for Evaluating Subsurface Vapor Intrusion into Buildings* (USEPA, 2004a).

[9] This table can be found on EPA Regions 3, 6, and 9 websites (http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm; http://www.epa.gov/earth1r6/6pd/rcra_c/pd-n/screen.htm; and http://www.epa.gov/region09/waste/sfund/prg/index.html).

2. BACKGROUND ON DERIVATION OF INHALATION TOXICITY VALUES

For all exposure routes, there are generally two approaches for deriving toxicity values. One involves the derivation of a reference value (e.g., RfC or RfD), while the other involves derivation of a predictive cancer risk estimate (e.g., an oral or inhalation CSF, such as an IUR). For the inhalation route, both approaches rely on EPA's *Inhalation Dosimetry Methodology* for the extrapolation of experimental concentrations to HECs. This extrapolation is described in Section 2.1 and its subsections. The approaches for deriving a toxicity value from the HEC are described in Sections 2.2 and 2.3 and differ depending on the type of toxicity value (e.g., RfC, IUR). This information is provided for background purposes only. **The procedures outlined in Section 2 are typically performed by IRIS chemical managers or by inhalation toxicologists at the National Center for Environmental Assessment's (NCEA's) Superfund Health Risk Technical Support Center (STSC) rather than as part of a baseline risk assessment.**

2.1 Application of Inhalation Dosimetry

The *Inhalation Dosimetry Methodology* recognizes a hierarchy of approaches that can be used for determining the HEC that is used to derive the RfC or IUR. Generally, the preferred approach is to use physiologically-based pharmacokinetic (PBPK) models.[10] With sufficient data, a PBPK model is capable of calculating the amount of the chemical that reaches the target organ in an animal from any exposure scenario and then estimating what human exposure would result in this same amount of chemical reaching the target organ (i.e., the HEC). PBPK models can also be used to derive continuous ECs from human and animal studies with less-than-continuous exposures. Because constructing a valid PBPK model is an information-intensive process that typically requires substantial chemical-specific data, this approach has rarely been used (USEPA, 2004b); an example can be found in the IRIS file for vinyl chloride (USEPA, 2000a). In cases where a complete PBPK model is not available, an intermediate model relying on certain chemical-specific data may be used (USEPA, 1994).[11]

If the database to support the preferred approach is inadequate, an alternative approach, called the Default Chemical Category-Specific Method can be used. This method incorporates the use of limited or categorical chemical-specific and physiological information. The default method is discussed below, followed by the procedures outlined in the *Inhalation Dosimetry Methodology* for deriving the RfC and IUR as they apply to the interpretation of animal and human data.

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[10] EPA defines PBPK models in the IRIS glossary as a model that estimates the dose to a target tissue or organ by taking into account the rate of absorption into the body, distribution among target organs and tissues, metabolism, and excretion (USEPA, 2008b). For further information about PBPK modeling, please refer to *Approaches for the Application of Physiologically Based Pharmacokinetic Models and Supporting Data in Risk Assessment* (USEPA, 2006a).

[11] The *Inhalation Dosimetry Methodology* recognizes the existence of alternate approaches in addition to the two presented in this guidance. The PBPK approach is generally preferred. In the absence of such a model, alternate models may be more optimal than the default approach when default assumptions or parameters can be replaced by more detailed, biologically-motivated descriptions or actual data, respectively. For instance, a model may be considered more optimal if it incorporates chemical or species-specific information or if it accounts for mechanistic determinants. See Table 3-6 in the *Inhalation Dosimetry Methodology* for more details on the hierarchy of approaches (EPA, 1994, page 3-40).

2.1.1 Default Approach - Extrapolation from Experimental Animal Data

The default method involves a two-step procedure that uses limited or categorical chemical-specific and physiological information to calculate the HEC. First, the chosen point of departure (POD) from the experimental data for a chemical is adjusted to derive a concentration intended to represent an equivalent dose under conditions of continuous exposure (7 days a week, 24 hours a day).[12] In the second step, this concentration is then multiplied by a Dosimetric Adjustment Factor (DAF) to generate the HEC. Further details on each step are outlined below.

2.1.1.1 Duration Adjustment to Continuous Exposure

Most of the inhalation studies of laboratory animals used to derive RfCs and IURs involve an exposure regimen of four to six hours per day, five to seven days per week, for 13 weeks or more (equivalent to 10 percent or more of the lifetime of the animal). The POD concentration from an animal study is mathematically adjusted to reflect an equivalent dose under conditions of continuous exposure.[13] Adjustment of duration to a continuous exposure scenario is regularly applied as a default procedure to studies with repeated exposures but not to single-exposure inhalation toxicity studies in animals (USEPA, 1994). Operationally, this is accomplished by applying a *c* x *t* product (where "*c*" is concentration, and "*t*" is duration of exposure) for both the number of hours in a daily exposure period and the number of days per week that the exposure is experienced. For example, if exposure in a particular study was 6 hours per day, 5 days per week, the experimental exposure is multiplied by 6/24 x 5/7 to calculate an equivalent continuous exposure. The general equation provided in the *Inhalation Dosimetry Methodology* (USEPA, 1994, Equation 4-2) for calculating duration-adjusted exposure levels in mg/m^3 for experimental animals is presented below.

$NOAEL_{[ADJ]}$ = E x D x W **(Equation 1)**

Where:

$NOAEL_{[ADJ]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach (e.g., LOAEL, LEC_{10}), adjusted for duration of experimental regimen;
E (mg/m^3) = the NOAEL or analogous exposure level observed in the experimental study;
D (h/h) = number of hours exposed/24 hours; and
W (days/days) = number of days of exposure/7days.

Using the example above, the assumption is that the product of *c* x *t*, not concentration alone, is associated with the toxicity observed. This is roughly equivalent to implying that if an effect occurs from a chemical at an exposure of 6 hours per day at 40 parts per million (ppm), that same effect will

[12] Examples of PODs include the no-observed-adverse-effect level (NOAEL); the lowest-observed-adverse-effect level (LOAEL); Benchmark Concentration, Lower confidence limit (BMCL); and the Lower limit on an Effective Concentration using a 10 percent response level (LEC_{10}). For definitions of the various PODs, please refer to the IRIS glossary (http://www.epa.gov/ncea/iris/help_gloss.htm).

[13] Continuous exposure refers to 24 hours per day, 7 days per week.

occur at an exposure of 24 hours per day at 10 ppm.[14] Note that this adjustment always produces a lower concentration value than that administered to experimental animals. Thus, as stated in *A Review of the Reference Dose and Reference Concentration Processes* (hereafter, the *RfD/RfC Review*), application of this procedure results in an automatic margin of protectiveness for chemicals for which concentration alone may be the more appropriate dose metric, and it reflects the maximum dose for chemicals for which total or cumulative dose is the appropriate measure (USEPA, 2002c). If a different procedure is used to calculate the continuous exposure, it should be fully discussed in the relevant technical support document for the chemical (e.g., IRIS profile, Provisional Peer Reviewed Toxicity Values (PPRTVs) Assessment). For additional discussion, including the uncertainties associated with this approach, see Section 4.3.2 of the *Inhalation Dosimetry Methodology* and Section 4.4.2.1 of the *RfD/RfC Review* (USEPA, 2002c).

2.1.1.2 Dosimetric Adjustment to Human Equivalent Concentration

Typically, the adjusted POD concentration from the animal study is next converted to an HEC using the following equation (USEPA, 1994, Equation 4-3):

$NOAEL_{[HEC]} = NOAEL_{[ADJ]} \times DAF$ **(Equation 2)**

Where:

$NOAEL_{[HEC]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an HEC;

$NOAEL_{[ADJ]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, adjusted for duration of experimental regimen; and

DAF = Dosimetric Adjustment Factor for the specific site of effects (e.g., respiratory tract region or extra-respiratory).

The DAF is typically based on ratios of animal and human physiologic parameters. The specific DAF used depends on the nature of the contaminant (e.g., particle or gas) and the target site where the toxic effect occurs (e.g., respiratory tract or a location in the body remote from the portal-of-entry). For example, the DAF can be based on either the Regional Gas Dose Ratio (RGDR), for gases with respiratory effects, or the Regional Deposited Dose Ratio (RDDR) for particles.

Table 2 provides information on the site of effects for the different chemical types. It also lists the physiologic parameters considered when calculating the DAF for specific regions of the body.[15] In addition, the table provides references to the equations from the *Inhalation Dosimetry Methodology* used in deriving the DAFs. Figure 1 provides a schematic of the human respiratory tract, illustrating each of the different regions.

[14] This assumption is based on Haber's Law, which states that "the incidence and/or severity of an adverse health effect depends on the total exposure to a potentially toxic substance. Total exposure (*K*) is the concentration of the substance (*c*) times the duration time of exposure (*t*), (i.e., $c \times t = K$)" (Gaylor, 2000).

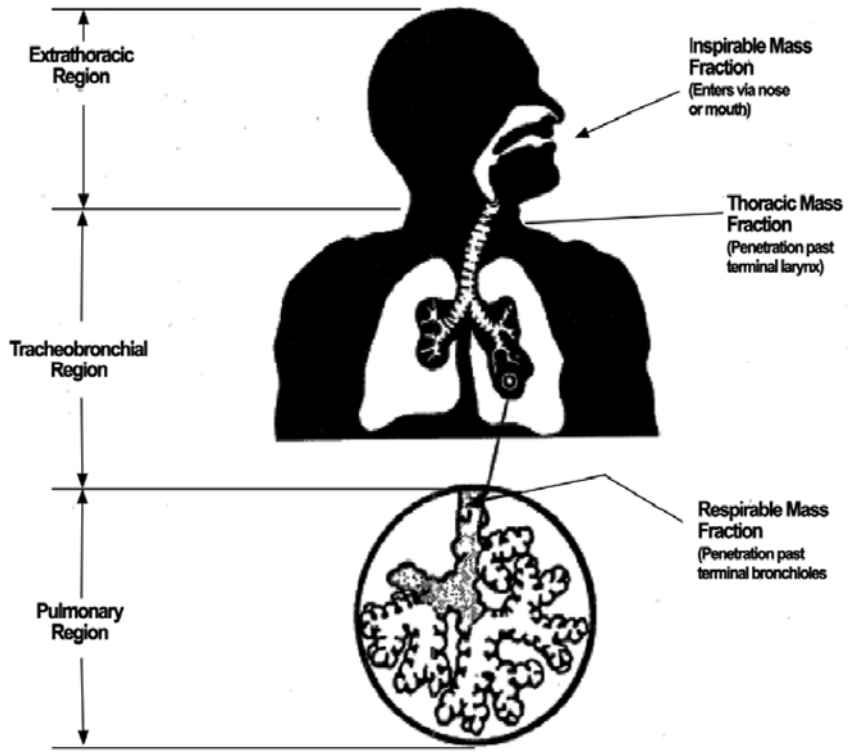
[15] The three main regions of the respiratory tract include the following: 1) Extrathoracic (includes nose, mouth, nasopharynx, oropharynx, laryngopharynx, and larynx); 2) Tracheobronchial (includes trachea, bronchi, and bronchioles); and 3) Pulmonary (includes respiratory bronchioles, alveolar ducts, alveolar sacs and the alveoli).

TABLE 2
CONTAMINANT PROPERTIES AND DOSIMETRIC ADJUSTMENT FACTORS[a]

Chemical Type	Site of Effects	Parameters Considered in Derivation of DAF for Regions of the Body[b]	DAF Equation Numbers in Inhalation Dosimetry Methodology[c]
Category 1 Gases (e.g., acrolein, hydrogen fluoride, chlorine)	Respiratory	-Minute volume (ETh, TB) -Surface area (ETh, TB, PU) -Mass transport coefficient (TB, PU) -Fraction of inhaled chemical penetrating the respiratory region (PU) -Alveolar ventilation rate (PU)	4-18 (ETh), 4-21 & 4-22 (TB), 4-28 (PU)
Category 2 Gases (e.g., acetonitrile, xylene, propanol, isoamyl alcohol)	Respiratory and Remote	-Mass transport coefficients (ETh, TB) -Blood:gas partition coefficient (ET, TB, ER) -Cardiac output (ETh, TB, ER) -Alveolar ventilation rate (PU) -Surface Area (PU) -Minute volume (ER)	4-18 (ETh), 4-21 & 4-22 (TB), 4-28 (PU), 4-48 (ER)[d,e]
Category 3 Gases (e.g., benzene, styrene)	Remote	Blood:gas partition coefficient (ER)	4-48[d]
Particles	Respiratory and Remote	-Minute volume (TOT, ER) -Surface area (TOT) -Fractional deposition of particle (TOT, ER) -Body weight (ER) -Inhaled concentration (ER)	4-14 (TOT), 4-15 (ER)

[a] Due to the complexities inherent in evaluating the health effects associated with exposure to gases, no definitive or comprehensive list of Category 1, 2, or 3 gases is available. Risk assessors should consult with an inhalation toxicologist in order to classify a specific gas as Category 1, 2, or 3, since there is overlap between the sites of effects and the parameters considered in deriving the DAF for different regions of the respiratory tract.
[b] Additional discussion of the terms used in this table can be found in the *Inhalation Dosimetry Methodology*.
[c] The *Inhalation Dosimetry Methodology* provides equations for deriving DAFs for the different contaminant categories. The equations listed in this table are the default equations for each specific region in the body.
[d] This refers to Equation 4-48 that is found on page 4-60 of the *Inhalation Dosimetry Methodology*.
[e] The equations presented for Category 2 gases in the *Inhalation Dosimetry Methodology* contain errors. Therefore, this table refers to the equations for Category 1 and 3 gases, which are expected to cover respiratory and remote effects from Category 2 gases.
Acronyms: ETh = Extrathoracic; TB = Tracheobronchial; PU = Pulmonary; ER = Extra-respiratory; TOT = Total respiratory system.

FIGURE 1
HUMAN RESPIRATORY TRACT



Source: EPA (1994), Figure 3-1, Page 3-5.

Category 1 gases are highly water-soluble and/or are rapidly irreversibly reactive in the respiratory tract (e.g., acrolein, hydrogen fluoride, chlorine). They do not significantly accumulate in the blood, and therefore their effects are usually exclusively respiratory (USEPA, 1994). The DAF for Category 1 gases consists of an RGDR and is based on the animal to human ratio of the minute volume (V_e) divided by the surface area (SA) of the region of the respiratory tract where the effect occurs.[16] See Appendix A, Sections 1, 2, and 3 of this guidance for examples of specific Category 1 DAF equations.

[16] For the purposes of this document, the V_e is defined as the total ventilation per minute and equals the product of the tidal volume (the air volume entering or leaving the lungs with a single breath) and the respiratory frequency.

Category 3 gases are relatively water-insoluble and are unreactive in the respiratory tract (e.g., benzene, styrene). Their toxicity is generally at sites remote to the respiratory tract (USEPA, 1994). The DAF for Category 3 gases is based on the ratio of the animal blood:gas partition coefficient ($H_{b/g\text{-}animal}$) and the human blood:gas partition coefficient ($H_{b/g\text{-}human}$). See Appendix A, Section 4 of this guidance for an example of a Category 3 DAF equation.

Category 2 gases are moderately water-soluble and may be rapidly reversibly reactive or moderately to slowly irreversibly reactive in respiratory tract tissue (e.g., acetonitrile, xylene, propanol, isoamyl alcohol). These gases have potential for significant accumulation in the blood, so they can exhibit both respiratory and remote toxicity (USEPA, 1994). The DAF for respiratory effects of Category 2 gases consists of an RGDR and is based on the animal to human ratio of the V_e and the SA of the region of the respiratory tract where the effect occurs, as for Category 1 gases. The DAF for extra-respiratory (ER) effects of a Category 2 gas is based on the ratio of the $H_{b/g\text{-}animal}$ and the $H_{b/g\text{-}human}$, as for Category 3 gases.

Particles also vary by solubility and reactivity. However, the default equations used to estimate the predicted regional deposition fractions for particles are based on non-soluble, non-hygroscopic particles (USEPA, 1994, Section 4.3.5.3). The DAF for a particle causing an effect in the respiratory tract is the $RDDR_r$. The $RDDR_r$ is based on the animal to human ratio of the V_e and the fractional deposition of the particle in that region (F_r), divided by the SA_r of the region where the effect occurs. This derivation, from the *Inhalation Dosimetry Methodology,* conservatively assumes that 100 percent of the deposited dose remains in the respiratory tract; clearance mechanisms are not considered. The DAF for a particle causing an ER effect, the $RDDR_{ER}$, is based on the animal to human ratio of the V_e and the total deposition of the particle in the entire respiratory tract (F_{total}), divided by BW (USEPA, 1994). The $RDDR_{ER}$ assumes that 100 percent of the deposited dose in the entire respiratory tract is available for uptake into the systemic circulation. See Appendix A, Section 5 for examples of specific particle DAF equations.

2.1.2 Default Approach - Extrapolation from Human Occupational Data

When human data are available to derive an RfC, duration adjustments are often required to account for differences in exposure scenarios (e.g., extrapolation from an 8 hour/day occupational exposure to a continuous chronic exposure). The default approach recommended by the *Inhalation Dosimetry Methodology* for adjusting the POD concentration (e.g., the no observable adverse effect level (NOAEL)) obtained from human study data is provided below in Equation 3 (USEPA, 1994, Equation 4-49).[17,18]

[17] If sufficient data are available, a PBPK model or intermediate approach using chemical-specific information may be employed in preference to the default method for extrapolating human occupational data to an HEC.

[18] EPA's IRIS glossary defines an adverse effect as the following: "A biochemical change, functional impairment, or pathologic lesion that affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge" (USEPA, 2008b).

$NOAEL_{[HEC]}$ = NOAEL x (VEho/VEh) x 5 days/7 days **(Equation 3)**

Where: $NOAEL_{[HEC]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an ambient HEC;
NOAEL (mg/m^3) = occupational exposure level (time-weighted average over an 8-hour exposure period);
VEho = human occupational default minute volume over 8 hours (10 m^3); and
VEh = human ambient default minute volume over 24 hours (20 m^3).

2.2 Derivation of the Inhalation Unit Risk

The default approach for determining predictive cancer risk recommended by EPA's *Guidelines for Carcinogen Risk Assessment* (USEPA, 2005a; hereafter, *Cancer Guidelines*) is a linear extrapolation from exposures observed in the animal or human occupational study.[19] This approach involves drawing a straight line from the POD to the origin. The default linear extrapolation approach is generally considered to be conservatively protective of public health, including sensitive sub-populations (USEPA, 2005a). The slope of this line is commonly called the slope factor, and when the units are risk per $\mu g/m^3$, it is also called the IUR. EPA defines an IUR in the IRIS glossary as "the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 $\mu g/m^3$ in air" (USEPA, 2008b). Equation 4 below presents a linear extrapolation from a POD of 10 percent response (LEC_{10}).[20]

$IUR = 0.1/LEC_{10[HEC]}$ **(Equation 4)**

Where: IUR $(\mu g/m^3)^{-1}$ = Inhalation Unit Risk; and
$LEC_{10[HEC]}$ ($\mu g/m^3$) = the lowest effective concentration using a 10 percent response level, dosimetrically adjusted to an HEC.

2.3 Derivation of the Reference Concentration

EPA defines an RfC in the IRIS glossary as "an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime" (USEPA, 2008b). The RfC is derived after a review of the health effects database for a chemical and identification of the most sensitive and relevant endpoint along with the principal study or studies demonstrating that endpoint. EPA Chemical Managers use UFs to account for recognized

[19] According to the *Cancer Guidelines*, "[a] nonlinear approach should be selected when there are sufficient data to ascertain the mode of action [MOA] and conclude that it is not linear at low doses and the agent does not demonstrate mutagenic or other activity consistent with linearity at low doses" (USEPA, 2005a, page 3-22). In addition, [l]inear extrapolation should be used when there are MOA data to indicate that the dose-response curve is expected to have a linear component below the POD" (USEPA, 2005a, page 3-21). This information will appear on the IRIS profile or other toxicological information source for a chemical. Chemicals with a mutagenic MOA are thought to pose a higher risk during early life. Procedures for assessing cancer risk from these chemicals are outlined in Section 5.1.

[20] The POD used in Equation 4 is an LEC_{10}, which is the lower 95 percent confidence limit on the concentration corresponding to a 10 percent response rate (i.e., the EC_{10}). Other PODs may be substituted for this value, which could be associated with alternative response levels (e.g., 1 percent, 5 percent).

uncertainties in the extrapolations from the experimental data conditions to an estimate appropriate to the assumed human scenario (USEPA, 1994). See Table 3 for a description of the standard UFs. The formula used for deriving the RfC from the HEC is provided below.

$RfC = NOAEL_{[HEC]}/(UF)$[1] **(Equation 5)**

Where: RfC (mg/m^3) = Reference Concentration
$NOAEL_{[HEC]}$ (mg/m^3) = The NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an HEC; and
UF = Uncertainty factor(s) applied to account for the extrapolations required from the characteristics of the experimental regimen.

[1] Some toxicological information sources for RfCs will incorporate an additional factor to account for deficiencies in the available data set, called a modifying factor (MF). In 2002, however, EPA published the *RfD/RfC Review,* which recommended that the use of MFs be discontinued because their purpose is "sufficiently subsumed in the general database UF" (USEPA, 2002c, page xviii). Therefore, RfCs published subsequent to this document will not include MFs.

TABLE 3
THE USE OF UNCERTAINTY FACTORS IN DERIVING AN INHALATION REFERENCE CONCENTRATION

Standard UFs	Processes Considered in the UF Purview
H = Human to sensitive human: Extrapolation of valid experimental results from studies using prolonged exposure to average healthy humans. Intended to account for the variation in sensitivity among the members of the human population.	-Pharmacokinetics/Pharmacodynamics -Sensitivity[2] -Differences in body weight (age, obesity) -Concomitant exposures -Activity pattern -Does not account for idiosyncrasies
A = Animal to human: Extrapolation from valid results of long-term studies on laboratory animals when results of studies of human exposure are not available or are inadequate. Intended to account for the uncertainty in extrapolating laboratory animal data to the case of average healthy humans.	-Pharmacokinetics/Pharmacodynamics -Relevance of laboratory animal model -Species sensitivity
S = Subchronic to chronic: Extrapolation from less-than-chronic exposure results on laboratory animals or humans when there are no useful long-term human data. Intended to account for the uncertainty in extrapolating from less than chronic NOAELs to chronic NOAELs.	-Accumulation/Cumulative damage -Pharmacokinetics/ Pharmacodynamics -Severity of effect -Recovery -Duration of study -Consistency of effect with duration
L = LOAEL to NOAEL: Derivation from a LOAEL instead of a NOAEL. Intended to account for the uncertainty in extrapolating from LOAELs to NOAELs.	-Severity -Pharmacokinetics/Pharmacodynamics -Slope of dose-response curve -Trend, consistency of effect -Relationship of endpoints -Functional vs. histopathological evidence -Exposure uncertainties
D = Incomplete to complete data: Extrapolation from valid results in laboratory animals when the data are "incomplete." Intended to account for the inability of any single laboratory animal study to adequately address all possible adverse outcomes in humans.[1]	-Quality of critical study -Data gaps -Power of critical study/supporting studies -Exposure uncertainties

[1] The *RfD/RfC Review* indicates that this UF accounts for the potential for deriving an underprotective RfD/RfC as a result of an incomplete characterization of the chemical's toxicity or if the existing data suggest that a lower reference value might result if additional data were available (considering both the lacking and available data for particular organ systems as well as life stage) (USEPA, 2002c).

[2] The *RfD/RfC Review* also stresses that susceptible populations and life stages are accounted for with this UF (USEPA, 2002c).

Source: USEPA, 1994, Table 4-9, page 4-77.

3. CHARACTERIZING EXPOSURE

3.1 Introduction

This section describes an approach for characterizing exposure in a baseline risk assessment that is consistent with the *Inhalation Dosimetry Methodology*. The approach involves the estimation of exposure concentrations (ECs) for each receptor exposed to contaminants via inhalation in the risk assessment. ECs are time-weighted average concentrations derived from measured or modeled contaminant concentrations in air at a site, adjusted based on the characteristics of the exposure scenario being evaluated.[21,22]

Equations for estimating ECs are provided below. This document does not provide default input values for the exposure parameters referenced in these equations. EPA recommends the use of site-specific exposure values consistent with the exposure pathways and receptors at a site wherever practicable and appropriate. If a risk assessor opts to rely on default exposure input values, current Superfund-supported values may be found at the exposure assessment portion of the Superfund website: (http://www.epa.gov/oswer/riskassessment/superfund_hh_exposure.htm).

3.2 Estimating Exposure Concentrations for Assessing Cancer Risks

The estimation of an EC when assessing cancer risks characterized by an IUR involves the CA measured at an exposure point at a site as well as scenario-specific parameters, such as the exposure duration and frequency.[23] The EC typically takes the form of a CA that is time-weighted over the duration of exposure and incorporates information on activity patterns for the specific site or the use of professional judgment. The equation for estimating an EC for use with an IUR is presented below.

[21] The default method for deriving inhalation toxicity values also involves calculating time-weighted ECs, as discussed in Sections 2.1.1.1 and 2.1.2.

[22] The ECs in this document are in units of $\mu g/m^3$. Inhalation toxicity values presented on IRIS are typically expressed in units of $\mu g/m^3$ or mg/m^3, which are mass units. Some regulatory contexts require the use of volumetric units such as ppm. The conversion from mass units to volumetric units depends on the molecular weight (MW) of the material as well as the ambient temperature and atmospheric pressure. To convert from ppm to mg/m^3, the following equation can be used: $\frac{ppm \times MW}{V} = mg/m^3$; where MW is the molecular weight of the gas and V is the volume of 1 gram molecular weight of the airborne contaminant. This is derived by the formula V = RT/P; where R is the ideal gas constant, T is the temperature in Kelvin (K = 273.16 + T°C) and P is the pressure in mm Hg. The value of R is 62.4 when T is in Kelvin, (K = 273.16 + T°C), the pressure is expressed in units of mm Hg and the volume is in liters. The value of R differs if the temperature is expressed degrees Fahrenheit (°F) or if other units of pressure are used (e.g., atmospheres, kilopascals).

[23] ECs are typically based on either estimated (i.e., modeled) or measured contaminant concentrations in air.

EC = (CA x ET x EF x ED)/AT **(Equation 6)**

Where: EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;
ET (hours/day) = exposure time;
EF (days/year) = exposure frequency;
ED (years) = exposure duration; and
AT (lifetime in years x 365 days/year x 24 hours/day) = averaging time

3.3 Estimating Exposure Concentrations for Calculating Hazard Quotients

When estimating ECs for non-cancer or cancer hazards characterized by an HQ, risk assessors should match each exposure scenario at a site to the appropriate EC equation, based on the scenario duration and frequency of exposure.[24] Figure 2 presents a flowchart to assist risk assessors with this process and provides recommended equations that can be used to estimate the EC for each type of scenario.[25] As shown in Figure 2, the recommended process for estimating ECs to be used in calculating an HQ involves the following three steps: 1) assess the duration of the exposure scenario; 2) assess the exposure pattern of the exposure scenario; and 3) estimate the scenario-specific EC.

3.3.1 Step 1: Assess Duration

The first step in the recommended process of estimating an EC for use in calculating an HQ involves assessing the duration of the exposure scenario at a site. Step 1 in Figure 2 indicates that the risk assessor first should decide whether the duration of the exposure scenario is generally acute, subchronic, or chronic. Toxicologists have long been aware that effects from a single or short-term exposure can differ markedly from effects resulting from repeated exposures. The response by the exposed person depends upon factors such as whether the chemical accumulates in the body, whether it overwhelms the body's mechanisms of detoxification or elimination, or whether it produces irreversible effects (Eaton & Klaassen, 2001). Therefore, ideally, the chemical-specific elements of metabolism and kinetics, reversibility of effects, and recovery time should be considered as part of this recommended process when defining the duration of a site-specific exposure scenario.

[24] Traditionally, the HQ approach was limited to non-cancer hazard assessment. However, the HQ approach may also be appropriate for carcinogens with a non-linear mode of action. The 2005 *Cancer Guidelines* state the following on this subject: "For cases where the tumors arise through a nonlinear mode of action, an oral reference dose or an inhalation reference concentration, or both, should be developed in accordance with EPA's established practice for developing such values … this approach expands the past focus of such reference values (previously reserved for effects other than cancer) to include carcinogenic effects determined to have a nonlinear mode of action" (USEPA, 2005a; page 3-24).

[25] Figure 2 was developed for the evaluation of inhalation exposures. While the concepts presented in this flowchart may be useful for assessing other exposure routes (e.g., oral or dermal), these other routes are beyond the scope of this document, and therefore, are not explicitly considered. Caution should be used when using Figure 2 to evaluate other exposure routes, as considerations beyond those outlined in the flowchart may apply (e.g., time to reach steady state for dermal exposures).

To the extent possible, exposure durations (EDs) evaluated in a site-specific risk assessment should be consistent with the ED represented by the toxicity value. However, frequencies or durations of human exposures often are not as clearly defined as those in animal studies with controlled exposures, particularly for intermittent exposures. For example, the emission of some volatile chemicals into the ambient air may vary with temperature and season, providing fluctuating exposures for humans living near the source. Therefore, risk assessors should use best professional judgment to determine if the ED in a given scenario is reasonably similar to the duration associated with the toxicity value. Risk assessors should describe the uncertainties associated with their choice of toxicity value in the risk characterization section of the risk assessment (see Section 9.2.2 of this document). For situations where duration-appropriate toxicity values are not available, please follow the procedures outlined in Section 4.2 and Appendix C of this document.

The specific definition for each exposure duration category may vary depending on the source of the toxicity value being used. For Tier 1 toxicity values obtained from EPA's IRIS database, acute exposures are defined as lasting 24 hours or less; subchronic exposures are defined as repeated exposures by the oral, dermal, or inhalation route for more than 30 days, up to approximately 10 percent of the human lifespan; and chronic exposures are defined as repeated exposures for more than approximately 10 percent of the human lifespan (USEPA, 2008b).[26, 27]

After deciding which duration the exposure scenario most closely matches, risk assessors should then proceed to Step 2, following the path of the selected duration. Note that if an acute duration is selected, risk assessors should proceed directly to Step 3 to estimate an acute EC for each acute exposure period.

3.3.2 Step 2: Assess Exposure Pattern

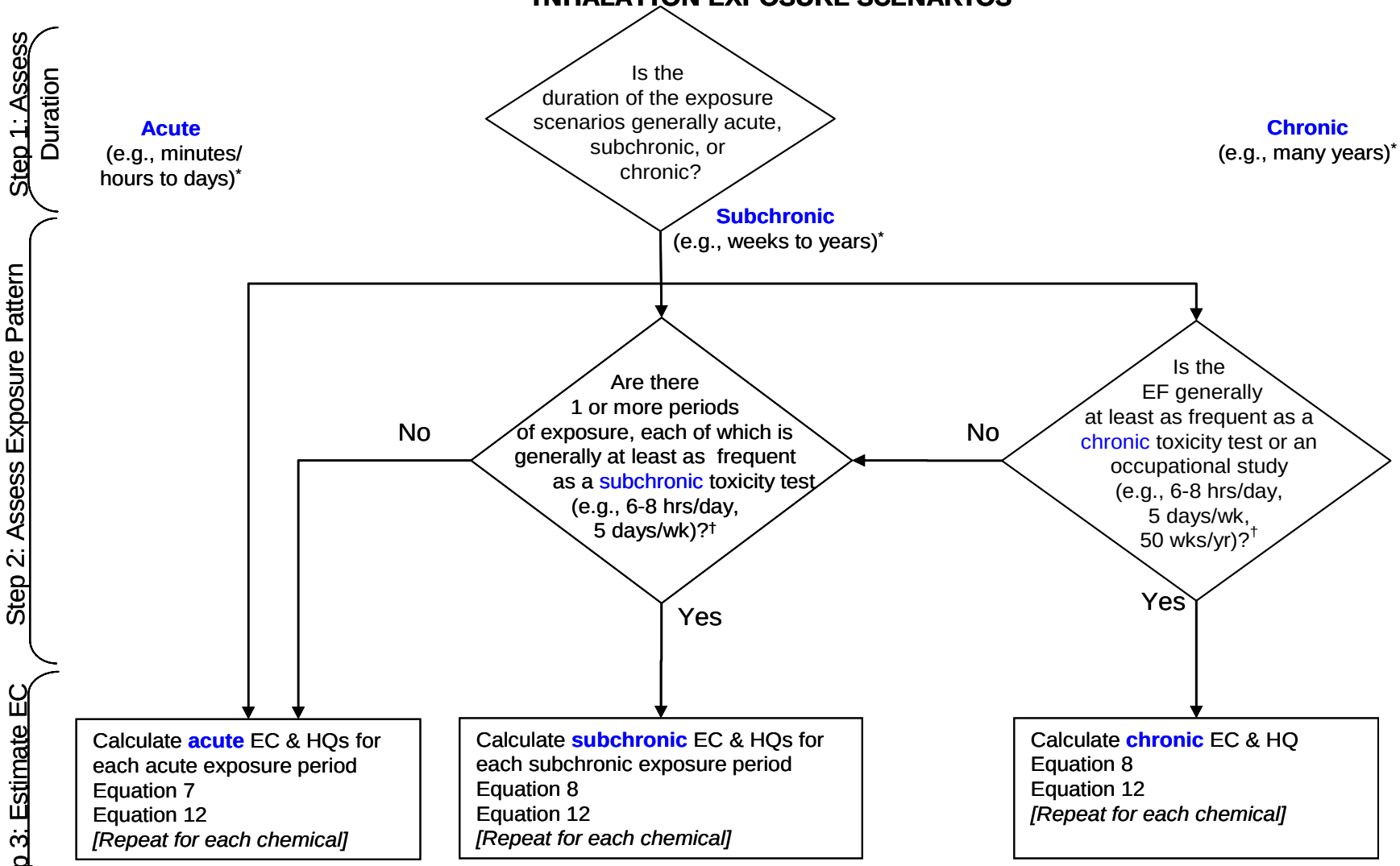
Step 2 of the recommended process for estimating an EC for use in a hazard quotient involves assessing the exposure pattern for each exposure scenario at a site. This entails comparing the exposure time and frequency at a site to that of a typical subchronic or chronic toxicity test.[28]

[26] Note that other sources of toxicity values may define exposures differently. For example, the Agency for Toxic Substances and Disease Registry (ATSDR) (which publishes Minimal Risk Levels (MRLs)) defines acute exposures as occurring from one to 14 days, intermediate exposures as greater than 14 to 364 days, and chronic exposures as 365 days or longer. However, the toxicity values are based on the same underlying toxicological concepts described in this section.

[27] Exposures with a duration lasting between 24 hours and 30 days should be treated as subchronic for the purposes of this document.

[28] Exposure regimens vary from study to study. Risk assessors should use best professional judgment to determine if the exposure pattern in a given scenario is reasonably similar to a typical regimen for a subchronic or chronic study.

FIGURE 2
RECOMMENDED PROCEDURE FOR DERIVING EXPOSURE CONCENTRATIONS AND HAZARD QUOTIENTS FOR INHALATION EXPOSURE SCENARIOS



* The specific definition for each duration category may vary depending on the source of the toxicity value being used. For Tier 1 toxicity values obtained from IRIS:
acute exposures are defined as those lasting 24 hours or less;
subchronic exposures are defined as repeated exposures for more than 30 days, up to approximately 10 percent of the life span in humans; and
chronic exposures are defined as repeated exposures for more than approximately 10 percent of the life span in humans (EPA, 2008b).
For the purposes of this document, short-term exposures, defined by the IRIS glossary as repeated exposures for more than 24 hours, up to 30 days, should be treated as subchronic.

† Exposure regimens vary from study to study. Risk assessors should use best professional judgment to determine if the exposure pattern in a given scenario is reasonably similar to a typical regimen for a chronic or subchronic study.

For exposure scenarios with a subchronic duration, risk assessors should follow the center path on the flowchart. Step 2 in this path asks whether there are one or more periods of exposure, each of which is generally as frequent as a subchronic toxicity test (e.g., 6-8 hours per day, 5 days per week). If the exposure scenario matches this description, risk assessors should proceed to Step 3 and estimate a subchronic EC for each subchronic exposure period. However, if the exposure pattern contains periods that are significantly shorter and/or involve significantly less frequent exposures than indicated in the flow chart, risk assessors should derive acute ECs for each of these exposure periods. If it is difficult to determine whether a specific exposure scenario is best modeled as a subchronic exposure or as a series of independent acute exposures, due to uncertainty in the time required to return to baseline following exposure, risk assessors may want to derive ECs using both approaches.

If the exposure scenario has a chronic duration, risk assessors should follow the right hand path on the flowchart. Step 2 in this path asks whether the exposure frequency (EF) is generally as frequent as a chronic animal toxicity test or a human occupational study (e.g., 6-8 hours per day, 5 days per week, for 50 weeks per year). If the exposure scenario matches this description, risk assessors should proceed to Step 3 and estimate a single chronic EC. However, if the scenario differs significantly from this pattern, risk assessors should proceed to the second question under the subchronic duration path and proceed as outlined above.

3.3.3 Step 3: Estimate Exposure Concentration

Step 3 of the recommended process involves estimating the EC for the specific exposure scenario based on the decisions made in Steps 1 and 2. For acute exposures, the EC is equal to the CA. Risk assessors can estimate an acute EC for each acute exposure period at a site using Equation 7. For longer-term exposures, risk assessors should take into consideration the exposure time, frequency, and duration for each receptor being evaluated as well as the period over which the exposure is averaged (i.e., the averaging time (AT)) to arrive at a time-weighted EC. If there are one or more exposure periods that are generally as frequent as a subchronic toxicity test, risk assessors should use Equation 8 to estimate a subchronic EC for each of these exposure periods. (Exposure periods with significantly less frequency should be treated as acute exposures.) If the exposure pattern is generally as frequent as a chronic toxicity test of an occupational study, risk assessors should use Equation 8 to estimate a single chronic EC for the duration of the exposure.

Acute Exposures

EC = CA **(Equation 7)**

Where: EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;

Chronic or Subchronic Exposures

EC = (CA x ET x EF x ED)/AT **(Equation 8)**

Where:
EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;
ET (hours/day) = exposure time;
EF (days/year) = exposure frequency;
ED (years) = exposure duration; and
AT (ED in years x 365 days/year x 24 hours/day) = averaging time

Note: If the duration of the exposure period is less than one year, the units in the above equation can be changed to the following: EF (days/week); ED (weeks/exposure period); and AT (hours/exposure period).

It is important to use the EC equation that most closely matches the exposure pattern and duration at a site. For instance, if the exposure pattern at a site consists of a series of short (e.g., 4-hour) periods of high exposure separated by several days of no exposure, the approach outlined above recommends estimating an acute EC for each acute exposure period. If the chronic EC equation (Equation 8) were to be used instead, the result would be an average EC value that may lead to an underestimate of risk since the inhaled concentrations could be higher than acute toxicity values during periods of exposure.

3.4 Estimating Exposure Concentrations in Multiple Microenvironments

When detailed information on the activity patterns of a receptor at a site is available, risk assessors can use these data to estimate the EC for either non-carcinogenic or carcinogenic effects. The activity pattern data describe how much time a receptor spends, on average, in different microenvironments (MEs), each of which may have a different contaminant concentration level.[29] By combining data on the contaminant concentration level in each ME and the activity pattern data, the risk assessor can calculate a time-weighted average EC for a receptor. Because activity patterns (and hence, MEs) can vary over a receptor's lifetime, EPA recommends that risk assessors pursuing the ME approach first calculate a time-weighted average EC for each exposure period characterized by a specific activity pattern (e.g., separate ECs for a school-aged child resident and a working adult resident). These exposure period-specific ECs can then be combined into a longer term or lifetime average EC by weighting the EC by the duration of each exposure period. The following sections further explain these two steps.

3.4.1 Using Microenvironments to Estimate an Average Exposure Concentration for a Specific Exposure Period

The ME approach can be used to estimate an average EC for a particular exposure period during which a receptor has a specified activity pattern. As a simplified example, a residential receptor may

[29] EPA defines a microenvironment in *Air Quality Criteria for Particulate Matter: Volume II* as a defined space that can be treated as a well-characterized, relatively homogeneous location with respect to pollutant concentration for a specified time period (e.g., rooms in homes, restaurants, schools, offices, inside vehicles, or outdoors) (USEPA, 2004b).

be exposed to a higher concentration of a contaminant in air in the bathroom for 30 minutes per day while showering, and exposed to a lower concentration in the rest of the house for the remaining 23.5 hours per day. In this case, risk assessors can use the CA value experienced in each ME weighted by the amount of time spent in each ME to estimate an average EC for the period of residency in that house using Equation 9.[30] This approach may also be used to address exposures to contaminants in outdoor and indoor environments at sites where both indoor and outdoor samples have been collected or where the vapor intrusion pathway has been characterized.

$$EC_j = \sum_{i=1}^{n} \left(CA_i \times ET_i \times EF_i\right) \times ED_j / AT_j \qquad \textbf{(Equation 9)}$$

Where:
EC_j ($\mu g/m^3$) = average exposure concentration for exposure period j;
CA_i ($\mu g/m^3$) = contaminant concentration in air in ME i;
ET_i (hours/day) = exposure time spent in ME i;
EF_i (days/year) = exposure frequency for ME i;
ED_j (years) = exposure duration for exposure period j; and
AT_j (hours) = averaging time = ED_j x 24 hours/day x 365 days/year.

3.4.2 Estimating an Average Exposure Concentration Across Multiple Exposure Periods

To derive an average EC for a receptor over multiple exposure periods, the average EC from each period (as calculated above in Equation 9) can be weighted by the fraction of the total exposure time that each period represents, using Equation 10. For example, when estimating cancer risks, the risk assessor may calculate a lifetime average EC where the weights of the individual exposure periods are the duration of the period, ED_j, divided by the total lifetime of the receptor. Alternatively, when estimating an HQ, risk assessors can use Equation 10 to calculate less-than-lifetime average ECs across multiple exposure periods. In that case, the AT will equal the sum of the individual EDs for all of the exposure periods.

$$EC_{LT} = \sum_{i=1}^{n} \left(EC_j \times ED_j\right) / AT \qquad \textbf{(Equation 10)}$$

Where:
EC_{LT} ($\mu g/m^3$) = long-term average exposure concentration;
EC_j ($\mu g/m^3$) = average exposure concentration of a contaminant in air for exposure period j;
ED_j (years) = duration of exposure period j; and
AT (years)[1] = averaging time.

[1] When evaluating cancer risk, the AT is equal to lifetime in years. When evaluating non-cancer hazard, the AT is equal to the sum of the EDs for each exposure period.

[30] If one or more MEs involve acute exposures, risk assessors should conduct a supplemental analysis comparing the CA for each of those MEs to a corresponding acute toxicity value to ensure that receptors are protected from potential acute health effects.

4. SELECTING APPROPRIATE TOXICITY VALUES

After characterizing the exposure scenarios and estimating ECs for each receptor at a site, the risk assessor should select appropriate inhalation toxicity values for each inhaled contaminant. For estimating cancer risks, this typically involves identifying and evaluating available published cancer potency estimates. For estimating HQs, this typically involves identifying and evaluating reference values that match the characterization of the exposure scenario from Figure 2 (i.e., acute, subchronic, or chronic reference values).

This section provides guidance for the selection of toxicity values appropriate for assessing risk under inhalation exposure scenarios. It describes sources for the most current inhalation data and provides guidance for proceeding when published inhalation toxicity data are not available.

4.1 Sources for Inhalation Toxicity Data

The OSWER Directive, *Human Health Toxicity Values in Superfund Risk Assessment* (USEPA, 2003), provides a recommended hierarchy of toxicological data sources to guide risk assessors when selecting appropriate toxicity values. This document sets out a recommended three-tiered framework for selecting human toxicity values. Tier 1 consists of EPA's IRIS, Tier 2 consists of EPA's PPRTVs, and Tier 3 includes other toxicity values as recommended by NCEA, such as the California EPA toxicity values, the Agency for Toxic Substances and Disease Registry's (ATSDR's) Minimal Risk Levels (MRLs), and Health Effects Assessment Summary Table (HEAST) toxicity values. Priority in Tier 3 should be given to sources that are the most current and those that are peer reviewed. Consultation with the Superfund Headquarters office is recommended regarding the use of Tier 3 values for Superfund response decisions when the contaminant appears to be a risk driver for the site.

The most up-to-date information on Superfund-supported cancer potency estimates and chronic and subchronic cancer and non-cancer reference values for inhaled contaminants are available on the Superfund risk assessment website (www.epa.gov/oswer/riskassessment/superfund_toxicity.htm). Superfund-recommended sources for acute non-cancer toxicity values can be found at www.epa.gov/oswer/riskassessment/superfund_acute.htm.[31]

In situations where the desired reference value (e.g., acute, subchronic, chronic) is not available, risk assessors may use a reference value based on the next longer duration of exposure as a conservative estimate that would be protective for a shorter-term ED (USEPA, 2002c). For example, if a risk assessor determines that an ED at a site is subchronic, but no subchronic toxicity value is available, a chronic RfC can be used to assess hazard.

EPA recommends that toxicity values published in Superfund-supported sources should generally be used in the risk equations presented in this guidance, without modification. This includes IURs on IRIS that were calculated from oral values using a default ventilation rate and BW (see Appendix B for a list of these chemicals). It is not generally appropriate to make adjustments to these values

[31] In selecting an acute toxicity value, risk assessors should consider the duration associated with their estimate of exposure (e.g., a 1-hour versus a 24-hour air sample). Use of a toxicity value specified for a longer duration than that of the exposure estimate may overestimate hazard, while the use of a shorter duration acute reference value may underestimate hazard.

based on IR and BW using the intake equation, because the amount of the chemical that reaches the target site through the inhalation pathway is not a simple function of these parameters (see Section 1.2). Use of the toxicity values listed in Appendix B should be noted in the uncertainty section of the risk assessment (see Section 9).

4.2 Recommended Procedures for Assessing Risk in the Absence of Inhalation Toxicity Values

The following section provides guidance on recommended procedures for situations where inhalation toxicity values are not available in any of the toxicity data sources described in Section 4.1.

If RfC and IUR values are not available for an inhaled contaminant, risk assessors should first contact NCEA's STSC for guidance.[32] Risk assessors working on Superfund sites can contact STSC to determine whether a provisional peer-reviewed toxicity value (PPRTV) exists for a contaminant; if not, the risk assessor, in cooperation with the appropriate EPA Regional office may request that STSC develop a PPRTV document or that STSC develop an inhalation toxicity value as a "consult". The latter would be specific to the site in question only. Additional information on STSC's current process for developing alternative toxicity values is described in Appendix C.

If STSC indicates that no quantitative toxicity information for the inhalation route is available, the risk assessor should conduct a qualitative evaluation of this exposure route. The risk assessor should discuss in the uncertainty section of the risk assessment report the implications of not quantitatively assessing risks due to inhalation exposures to chemicals lacking inhalation toxicity data. See the section on Risk Characterization (Section 9) in this guidance for more information.

Performing simple route-to-route extrapolation without the assistance of STSC is generally not appropriate because hazard may be misrepresented when data from one route are substituted for another without any consideration of the pharmacokinetic differences between the routes (USEPA, 1998). The following circumstances, outlined in the *Inhalation Dosimetry Methodology* (page 4-6), are specific examples of situations when route-to-route extrapolation from oral toxicity values might not be appropriate, even for use during screening:

- When groups of chemicals are expected to have different toxicity by the two routes – for example, metals, irritants, and sensitizers;
- When a first-pass effect by the respiratory tract is expected;
- When a first-pass effect by the liver is expected;
- When a respiratory tract effect is established, but dosimetry comparison cannot be clearly established between the two routes;
- When the respiratory tract was not adequately studied in the oral studies; and
- When short-term inhalation studies, dermal irritation, in vitro studies, or characteristics of the chemical indicate the potential for portal-of-entry effects at the respiratory tract, but studies themselves are not adequate for inhalation toxicity value development.

[32] All contact with STSC should be performed by an EPA regional risk assessor. States and other entities should first contact their EPA regional risk assessor with questions on inhalation toxicity values. Regional risk assessors can then contact STSC on their behalf.

The *Cancer Guidelines* (USEPA, 2005a) includes the following statement regarding route-to-route extrapolation:

> "When a qualitative extrapolation can be supported, quantitative extrapolation may still be problematic due to the absence of adequate data. The differences in biological processes among routes of exposure (oral, inhalation, dermal) can be great because of, for example, first-pass effects and different results from different exposure patterns. There is no generally applicable method for accounting for these differences in uptake processes in a quantitative route-to-route extrapolation of dose-response data in the absence of good data on the agent of interest. Therefore, route-to-route extrapolation of dose data relies on a case-by-case analysis of available data" (page 3-10).

5. ESTIMATING RISKS

This section provides updated equations recommended for estimating excess cancer risks and HQs from inhaled contaminants of concern at Superfund sites. Please see Section 8.2.1 of *RAGS, Part A* for further information about how to interpret calculated excess cancer risks and HQs.

5.1 Cancer Risks Characterized by an Inhalation Unit Risk

The excess cancer risk for a receptor exposed via the inhalation pathway can be estimated with the following equation:

Risk = IUR x EC **(Equation 11)**

Where: IUR $(\mu g/m^3)^{-1}$ = Inhalation Unit Risk; and
EC $(\mu g/m^3)$ = exposure concentration (See Equation 6).

When estimated ECs are above the POD used for the low dose extrapolation described in Section 2.3, a linear concentration-response relationship may not hold.[33] In such situations, the risk assessor should not use toxicity values developed through low dose extrapolation techniques. Instead, the risk assessor may report semi-quantitative risk estimates (e.g., risks are greater than 10^{-2}) or estimate risk using the original model underlying the toxicity value, which can be found in the technical support document for the value (e.g., IRIS profile, PPRTV Assessment).

When estimating cancer risks for children, risk assessors should be aware of chemicals that pose a higher risk of cancer when exposure occurs during early life. If evidence exists suggesting differences in risk across age groups for a chemical, this typically will be considered in the derivation of the toxicity value and described in the chemical's technical support document.

[33] Reviews of chemical-specific IRIS files indicate that the risk level corresponding to the concentration level above which the IUR should not be used often falls at or near 10^{-2}. However, this risk level varies by chemical and, therefore, risk assessors should refer to the toxicity value's technical support document for information on the concentration range for which the IUR was intended to be used.

Chemicals that have been determined to cause cancer by a mutagenic mode of action (MOA) are thought to pose a higher risk during early life. An EPA-recommended procedure exists for assessing risks from these chemicals. Figure 3 summarizes the recommendations of the *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (USEPA, 2005b; hereafter *Supplemental Cancer Guidelines*) on how to adjust childhood risk calculations to account for chemicals with a mutagenic MOA for carcinogenicity. Please refer to the *Supplemental Cancer Guidelines* (USEPA, 2005b) for a list of chemicals with a mutagenic MOA that were used in the development of that document.

In addition, EPA's website for the "Handbook for Implementing the Supplemental Cancer Guidance at Waste and Cleanup Sites" contains an up-to-date list of chemicals that EPA has determined to have a mutagenic MOA (http://www.epa.gov/oswer/riskassessment/sghandbook/index.htm). As chemicals receive new assessments for mutagenicity, this information will appear in the IRIS profile or PPRTV assessment.

FIGURE 3
GUIDANCE ON ASSESSING RISK FROM EARLY-LIFE EXPOSURES FOR CHEMICALS ACTING BY A MUTAGENIC MODE OF ACTION FOR CARCINOGENICITY

If a chemical has been determined to cause cancer by a mutagenic MOA, it is possible that exposures to that chemical in early-life may result in higher lifetime cancer risks than a comparable duration adult exposure.

In risk assessments of exposure to chemicals for which a mutagenic MOA for carcinogenicity has been determined by EPA and a linear low-dose extrapolation performed, one of the following generally pertains:

1) If chemical-specific data on susceptibility from early-life exposures were available for derivation of CSFs, those slope factors are used for risk characterization, and Age Dependent Adjustment Factors (ADAFs) are not applied.
2) If chemical-specific data on susceptibility from early-life exposures were not available, the ADAFs are applied in calculating or estimating risks associated with early-life exposures (USEPA, 2005c).

If the latter case applies, the *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (USEPA, 2005b) recommends the following default ADAFs be applied in risk assessments:

- 10-fold adjustment for exposures during the first 2 years of life;
- 3-fold adjustment for exposures from ages 2 to <16 years of age; and
- No adjustment for exposures after turning 16 years of age.

In such cases, Equation 11 can be altered to include the ADAFs in the following way:

$$Risk = (IUR \times EC_{<2} \times ADAF_{<2}) + (IUR \times EC_{2\text{-}16} \times ADAF_{2\text{-}16}) + (IUR \times EC_{>16})$$

Sources: USEPA, 2005b and USEPA, 2005c.
Note: All communications and factsheets pertaining to the implementation of the 2005 *Cancer Guidelines* can be found at www.epa.gov/osa/spc/cancer_guidelines.htm.

5.2 Hazard Quotients

The HQ for the inhalation pathway can be calculated with the following general equation:

HQ = EC/(Toxicity Value[1] x 1000 µg/mg) **(Equation 12)**

Where: HQ (unitless) = Hazard Quotient;
EC ($\mu g/m^3$) = exposure concentration (See Equations 7 or 8);
Toxicity Value (mg/m^3) = Inhalation toxicity value (e.g., RfC) that is appropriate for the exposure scenario (acute, subchronic, or chronic).

[1] Risk assessors should refer to the flowchart (Figure 2) to select an appropriate inhalation toxicity value for the exposure scenario at a site in order to calculate the HQ.

6. EXAMPLE EXPOSURE SCENARIOS

This section of the guidance includes examples of the types of exposure scenarios risk assessors may encounter when evaluating inhalation exposures at waste sites. Each scenario includes sample values for exposure parameters and reviews the process of estimating the EC and risks for cancer and other health effects. These examples are provided for illustrative purposes only and are not representative of every exposure scenario that could be encountered at a site. Furthermore, risk assessors should use site-specific values for exposure parameters if practicable when estimating ECs and risk levels or HQs. This would typically require some information on activity patterns for the specific site or the use of professional judgment. If default values are to be used for certain exposure parameters, please consult the Superfund website for up-to-date information on Superfund-recommended default exposure parameters.[34]

6.1 Residential Receptor

An example of a residential scenario could consist of inhalation exposure for up to 24 hours per day, up to 350 days per year for 6 to 30 years. When estimating cancer risk for this type of scenario, Equation 6 is recommended to calculate an EC and Equation 11 is recommended to estimate risk. For estimating hazard quotients for cancer or non-cancer effects, this scenario can be evaluated using the steps outlined in Figure 2. The duration of this scenario ranges from 6 to 30 years, which can be considered chronic (because it consists of repeated exposures for approximately 10 percent of a receptor's lifespan). The frequency of this scenario is generally as frequent as a chronic toxicity test and therefore Equation 8 is recommended to derive a chronic EC and Equation 12 with a chronic toxicity value is recommended to calculate an HQ. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 to estimate ECs to use in estimating cancer risks or HQs.

When assessing the risk under the residential scenario for children, the risk assessor should keep in mind that exposure parameters, specifically those related to activity patterns (e.g., exposure time, frequency, and duration) may be different for children and adults at the same site. For example, due

[34] http://www.epa.gov/oswer/riskassessment/superfund_hh_exposure.htm.

to outdoor play patterns, children may spend more time near the source of contamination than adults, and thus would have higher exposure time and/or exposure frequency values than adults living in the same location.[35] For indoor vapor intrusion from the subsurface, very young children might be more highly exposed due to substantial time spent indoors.

Beyond the consideration of activity patterns, MEs, and chemicals with a mutagenic MOA for carcinogenicity (as described in Section 5.1), no additional adjustments to account for specific child receptors should be made to the default values. Appendix A of this document is intended to illustrate that the use of default values sufficiently covers age-related variation in DAF or HEC values derived using the EPA *Inhalation Dosimetry Methodology's* default approach.

6.2 Commercial-Industrial/Occupational Receptor

An example of a commercial-industrial or occupational inhalation exposure scenario could be characterized by full-time workers (e.g., 8 hours per day, 5 days per week) in an indoor setting, such as an office building, exposed via vapor intrusion of subsurface contamination on a daily basis for 5 to 25 years. When estimating cancer risk for this type of scenario, Equation 6 is recommended to calculate an EC and Equation 11 is recommended to estimate risk. Following the flowchart in Figure 2, the duration and exposure pattern of this scenario would typically be considered chronic. Therefore, Equation 8 is recommended to derive a chronic EC and Equation 12 is recommended (with a chronic RfC) when calculating an HQ for cancer or non-cancer effects. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 when deriving ECs to use in estimating cancer risks or HQs. Exposure parameters should be adjusted to consider the exposure time, frequency and duration for this scenario, which may differ from a residential scenario. Risk assessors should also use appropriate exposure parameters for outdoor workers who, similar to children, may spend more time near a source of contamination than indoor workers.

6.3 Construction Worker

One example of a construction worker scenario could involve a long-term project (1-2 years) with workers exposed regularly to contaminant vapors and fugitive dust (8 hours per day, 5 days per week). When estimating cancer risk for this type of scenario, Equations 6 and 11 are recommended to calculate an EC and the risk estimate, respectively. Following the flowchart in Figure 2, the duration of this exposure scenario would typically be considered subchronic. In addition, this exposure is generally as frequent as a subchronic toxicity test. Therefore, Equation 8 is recommended to derive a subchronic EC, and Equation 12 is recommended for use with a subchronic toxicity value to calculate the HQ. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 when deriving ECs to use in estimating cancer risks or HQs.

6.4 Trespasser/Recreational Receptor

An example trespasser/recreational scenario could consist of an exposure of 1 to 2 hours per day, for 100 days per year or less. When estimating cancer risk for this type of scenario, Equations 6 and 11

[35] For additional information about early-lifestage age groups to consider when assessing children's exposure to environmental contaminants, please consult EPA's *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (EPA, 2005d).

are recommended to calculate an EC and the risk estimate, respectively. Following the steps in Figure 2 for cancer or non-cancer effects characterized by an RfC, each exposure period should be assessed separately because this exposure lasts only one to two hours each day for an average of two days per week. Therefore, Equation 7 is recommended to derive acute ECs for each exposure period. In addition, Equation 12 is recommended for use with an acute toxicity value to calculate HQs for each exposure period.

7. TARGET CONCENTRATIONS FOR SCREENING ANALYSIS OF INHALATION PATHWAYS

For purposes of this guidance, risk-based screening levels are values that may be compared to the contaminant concentration in air to help risk assessors identify potential contaminants of concern. Screening levels can also be calculated for comparison with samples from source media at a site, such as soil. Screening levels are generally not appropriate for use as clean-up levels; they are intended to aid in initial evaluation of contaminants and exposure pathways of concern prior to proceeding with a baseline risk assessment.[36] If contaminant concentrations in air exceed the risk-based screening levels appropriate for the receptor population of interest, risk assessors should gather site-specific information to determine the need for any remedial action. The following sections outline a recommended approach for calculating screening levels in air as well as source media.

7.1 Target Contaminant Concentrations in Air

The equations recommended for estimating ECs and risk (Equations 6 through 12) can be used to calculate target contaminant concentrations in air by following the four steps outlined below in Table 4.[37]

If air samples from a site are found to be below the target concentration, the risk assessor can generally conclude that this pathway does not pose an unacceptable level of risk from the contaminant. If the concentrations are found to exceed the screening levels, the risk assessor should evaluate the inhalation pathway further by gathering additional site-specific data on contaminant levels, site conditions, and receptor characteristics.

7.2 Screening Levels for Other Media

Inhalation risk-based screening levels may also be calculated for media other than air, including soils, tap water, soil gas, and ground water. The soil gas and ground water values may be derived specifically to address concerns about vapor intrusion from subsurface contamination into indoor spaces.

[36] EPA regions, states, or other agencies may support unique screening levels for specific purposes that may differ from the method presented in this document. Generally, when using screening levels it is important that risk assessors understand the target risks, toxicity, and exposure assumptions as well as migration-attenuation assumptions on which they are based, and to apply them for their intended use.

[37] Target contaminant concentrations in air calculated according to the procedure outlined in this document are generally protective for direct inhalation exposures. This process should not be used to calculate concentrations in air to be protective of indirect exposures (e.g., ingestion of crops contaminated through air delivery or vapor phase transfer, ingestion of livestock or fish contaminated indirectly through air deposition or vapor phase transfer).

TABLE 4 RECOMMENDED PROCEDURE FOR CALCULATING RISK-BASED SCREENING CONCENTRATIONS FOR CONTAMINANTS IN AIR		
	Cancer Risk-Based	**Hazard-Based**[1]
Step 1: Select Target Levels	Select target cancer risk (e.g., 1×10^{-6}).	Select target HQ (e.g., 1).
Step 2: Identify Toxicity Value[2]	Identify inhalation cancer potency value (e.g., IUR). If none exists, proceed with hazard-based screening level calculation.	Identify inhalation reference value (e.g., RfC) to match exposure scenario (acute, subchronic, or chronic). If none exist, proceed with cancer screening level calculation.
Step 3: Calculate CA	Using target cancer risk from Step 1 along with the receptor- and scenario-specific exposure parameter values, calculate CA; the following equation is recommended: CA = (AT x Target Risk)/(IUR x ET x EF x ED)	Using target HQ from Step 1 along with the receptor- and scenario-specific exposure parameter values, calculate CA; the following equation is recommended: CA = (AT x Target HQ x RfC x 1000 µg/mg)/(ET x EF x ED)
Step 4: Select Screening Concentration	Select minimum of predicted cancer risk- and hazard-based values as screening concentrations.[3] Repeat for each receptor/scenario combination of interest.	

[1] Hazard-based screening concentrations are typically derived from reference values such as RfCs. These values may be available for non-cancer effects but may include cancer, if a nonlinear MOA is thought to operate for a chemical.
[2] If no inhalation toxicity value is available for a chemical, contact STSC for further direction on how to proceed.
[3] Screening levels estimated from the equations presented in Step 3 could yield concentrations that exceed the maximum possible vapor concentration for a chemical. In such cases, it may be useful to calculate the maximum possible vapor concentration of the pure contaminant at the temperature of interest, using the following formula: $C_{max} = S \times H \times 10^3$ L/m^3, where S = solubility at 25° C (or temperature of interest) and H (unitless) = Henry's Law Constant at 25° C (or temperature of interest). This equation is based on an established relationship (see, for example, Schwartzenbach et al. 1993), that allows the Henry's Law Constant to be estimated as the ratio of a compound's vapor pressure and aqueous solubility for compounds that are slightly to moderately soluble in water. When the dimensionless Henry's Law constant, H, is used, the relationship described above can be used to calculate the vapor concentration of a saturated solution of a given compound, assuming equilibrium between the vapor and aqueous phases.

7.2.1 Soil Screening Levels

When evaluating risk in a source medium, such as soil, it is typically possible to calculate screening levels for that medium that are expected to be protective of inhalation exposures based on the expected transfer of a contaminant from the source medium to the air. Soil Screening Levels (SSLs) can be described as "risk-based soil concentrations derived for individual chemicals of concern from standardized sets of equations. These equations combine EPA chemical toxicity data with parameters defined by assumed future land uses and exposure scenarios, including receptor characteristics and potential exposure pathways" (USEPA, 2002b). These SSLs may be used for screening analyses and may serve as the basis for the development of Preliminary Remediation Goals (PRGs). Refer to the *Soil Screening Guidance* (USEPA, 1996) and the *Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites* (USEPA, 2002b) for recommended equations that can be used to calculate SSLs for volatilization of chemicals from soil to air and for particulate emissions.

7.2.2 Tap Water Screening Values

Contaminated tap water may pose risk by the inhalation route if the contaminants present are volatile. Screening levels can be calculated for tap water that account for inhalation exposures resulting from the household use of water (e.g., showering, laundering, dishwashing). Risk assessors should consult their local EPA regional risk assessor for direction on how to calculate appropriate screening levels for tap water.

7.2.3 Soil Gas or Ground Water Screening Values for Vapor Intrusion

If there is concern at a site about the possibility of migration of vapor-forming chemicals from contaminated soil gas or ground water into the indoor air of overlying buildings ("vapor intrusion"), screening values can be calculated for these media. Risk assessors should first follow the procedure outlined in Section 7.1 and Table 4 to calculate a risk-based target concentration for the contaminant in air.

For the calculation of a soil gas screening-level concentration, the target air concentration is then divided by an assumed screening-level attenuation factor. The attenuation factor (the ratio of indoor air divided by subsurface source concentration) represents the factor by which subsurface vapor concentrations migrating into indoor air spaces are reduced due to a variety of attenuating mechanisms.

For the calculation of a ground water screening-level concentration, the target air concentration is divided by an assumed screening-level attenuation factor, and the resulting soil gas concentration is converted to a corresponding ground water concentration, assuming equilibrium between the aqueous and vapor phases at the water table.

Risk assessors should consult their local EPA regional risk assessor for direction on how to calculate appropriate screening levels for soil gas and ground water when vapor intrusion is an issue at a site.

8. DEVELOPING AGGREGATE AND CUMULATIVE RISK ESTIMATES

EPA's current approach to estimating cumulative risk or hazard at a site from multiple chemicals, set forth in *RAGS, Part A* (USEPA, 1989), is not affected by the *Inhalation Dosimetry Methodology* and therefore is not being updated at this time. In addition, the aggregation of risks and hazards across multiple exposure routes should remain unchanged. The recommended approaches for aggregating risk and hazard estimates are outlined below.

8.1 Estimating Cumulative Risks and Hazards Across Multiple Chemicals

The recommended method for estimating cumulative risk and hazard at a site from exposure to multiple chemicals is described in *RAGS, Part A*, Section 8.2.2. This method is based on the default approaches described in *Guidelines for the Health Risk Assessment of Chemical Mixtures* (USEPA, 1986). Additional information on this method was subsequently published in the *Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures* (USEPA, 2000b). The recommended methods to use with quantitative cancer risk estimates as well as with HQs are outlined below.

8.1.1 Cancer Risks

When evaluating predicted cancer risks from multiple contaminants, risk assessors should estimate the cancer risk for each substance and then sum these risks. This yields an estimate of total cancer risk, which represents the cumulative predicted cancer risk for the chemicals at a site.

Risk assessors should note, however, that this recommended method assumes "independence of action by the compounds involved (i.e., that there are no synergistic or antagonistic chemical interactions and that all chemicals produce the same effect, i.e., cancer)" (USEPA, 1989). In addition, this simple additive approach is generally most appropriate for total cancer risks less than 0.1. If these assumptions are incorrect, over- or under-estimation of actual multiple-substance risk could result (USEPA, 1989).

8.1.2 Hazard Quotients

When the evaluation involves multiple chemicals assessed via HQs, risk assessors typically first calculate the HQ for each substance, and then sum the individual HQ values. This generally yields an estimated hazard index (HI) for the multiple chemicals assessed via a hazard-based approach. Separate HIs should be calculated for each type of exposure period (i.e., chronic, subchronic, acute). If an HI is greater than 1, it is generally appropriate to derive separate HIs for each target organ of concern (for more information, see *RAGS, Part A*, page 8-14).[38] When multiple acute exposures are present at a site, risk assessors should evaluate each acute exposure event separately. Hazards from multiple chemicals generally should be summed only when the exposures to these chemicals occur simultaneously.[39]

8.2 Aggregating Risk and Hazard Quotients Across Exposure Routes

Guidance for combining the multi-chemical risk estimates and hazard quotients across exposure pathways is described in *RAGS, Part A*, Section 8.3 (USEPA, 1989). In order to determine whether risks or HIs should be combined across exposure pathways, risk assessors should first identify reasonable exposure pathway combinations. Then, risk assessors should examine whether it is likely that the same individuals would consistently face the reasonable maximum exposure (RME) by more than one pathway.

[38] This recommended method assumes that "the dose for each individual component is at a level at which effects are not expected to occur, be observable, or be of concern; however, when the doses are combined, effects of concern may be expected or observed in response to the higher dose level of the mixture" (EPA, 2000b, page 12). Another assumption of the HI approach is that the compounds induce the same effect by the same mechanism of action. Therefore, "application of the HI equation to a number of compounds that are not expected to induce the same type of effects or that do not act by the same mechanism, although appropriate as a screening-level approach, could overestimate the potential for effects" (EPA, 1989, page 8-14). This is generally less of a concern if one to two substances are responsible for driving the HI above 1.

[39] In cases where a single chemical is present at a site and receptors are exposed through a series of acute exposure events, the highest single EC should be compared to an acute reference value of the appropriate duration to assess hazard.

The recommended approach for estimating excess cancer risk from exposure via multiple routes is to first estimate cancer risk from each exposure pathway and then sum across the multiple routes.[40]

For the effects assessed via a reference value, risk assessors should calculate the HI for each exposure pathway and sum across the multiple routes. Separate total HIs should be calculated for each type of exposure period (i.e., chronic, subchronic or acute). If the HI exceeds one, there may be concern for potential adverse effects and risk assessors should consider deriving separate HIs for each target organ of concern.

9. RISK CHARACTERIZATION

Risk characterization is the final, summarizing step in conducting a risk assessment. Generally, the purpose of the risk characterization section of a report is to:[41]

- Describe the key findings of the risk assessment in a transparent manner, including identifying hazard, characterizing the dose-response relationship, and describing receptor exposures;
- Identify and describe the scientific and policy assumptions used in the assessment;
- Characterize uncertainties in results; and
- Provide an overall conclusion about the risks present at a site (USEPA, 2000c).

A well-crafted risk characterization section puts risk calculations into context for risk managers so that they may effectively weigh and interpret risk assessment results (i.e., it is the interface between risk assessment and risk management). A few of the key issues and uncertainties involved in calculating risks from inhalation exposures are outlined below.

9.1 Highly Exposed or Susceptible Populations and Life Stages

EPA recommends that the risk characterization portion of the risk assessment explain any particular susceptibilities to inhaled toxicants or potential for increased inhalation exposures among the various receptor groups at a site.[42] We discuss below two possible examples, children and worker receptors, though this discussion could apply to other receptor characteristics as well (e.g., age, disease, gender, genetic characteristics).

9.1.1 Children

One population group that could potentially be more highly exposed to inhalation exposures at a site is children. As discussed in Section 6.2, exposure parameters related to activity patterns (e.g., exposure time, frequency, and duration) and MEs, may vary across age groups. For example, due to outdoor play patterns, children may spend more time near the source of contamination than adults,

[40] Note that this approach is generally most appropriate for total cancer risks of less than 0.1 (EPA, 1989).

[41] For specific information on the format of risk characterizations, refer to *Elements to Consider when Drafting EPA Risk Characterizations* (EPA, 1995c).

[42] EPA's IRIS glossary defines susceptibility as the following: "Increased likelihood of an adverse effect, often discussed in terms of relationship to a factor that can be used to describe a human subpopulation (e.g., life stage, demographic feature, or genetic characteristic)" (EPA, 2008b).

and thus would have higher exposure time and/or exposure frequency values than adults living in the same location. Therefore, it is important to carefully describe site-specific exposures to children, and assumptions made in risk calculations.[43]

If chemical-specific data on susceptibility to the toxic effects from early life exposures are available, these data are considered when developing toxicity values that specifically address differential toxicity to the young (e.g., vinyl chloride) (USEPA, 2005c). Toxicity values derived using the default approach from the *Inhalation Dosimetry Methodology* are developed for the human population as a whole, including sensitive subgroups. Therefore, as described in Section 6 of Appendix A, no quantitative adjustment of toxicity values derived using the default approach in the *Inhalation Dosimetry Methodology* is recommended for specific age groups to account for different ventilation rates or body weights of specific age groups.

When evaluating risk to carcinogenic chemicals with a demonstrated mutagenic MOA but which lack chemical-specific information on susceptibility from early life exposures, EPA recommends a quantitative adjustment of the toxicity value to account for early life susceptibility, as described in the *Supplemental Cancer Guidelines* (see USEPA, 2005b & 2005c; and Section 5.1 of this guidance for further information).

9.1.2 Workers

Workers could have increased exposure under certain occupational scenarios. Some outdoor workers might spend more time near a source of contamination in the course of their job and this should be reflected in adjustments to the exposure parameters (e.g., ET, Exposure Frequency (EF), and ED) describing the worker exposure scenario. Toxicity values derived using the *Inhalation Dosimetry Methodology* are developed for the human population as a whole, including sensitive populations and life stages. In the default *Inhalation Dosimetry Methodology* approach, typical variation in IRs between periods of high activity and rest is considered. However, if workers have especially high levels of exertion with correspondingly high ventilation rates, these workers could be at the upper end of the risk range, particularly if they are exposed to Category 1 gases, which have direct effects in the respiratory tract. This implication should be recognized in the risk characterization section.

9.2 Uncertainties in Inhalation Risk Assessment

This guidance recommends including an assessment of the key uncertainties that may significantly impact risk estimates for inhaled chemicals. This should ensure transparency, clarity, reasonableness and consistency in risk assessments, as recommended by EPA's *Policy for Risk Characterization* (USEPA, 1995a). Other sources of uncertainty may be present and other EPA documents provide guidance on characterizing uncertainty in risk the assessment process (USEPA, 1992, 1995a, 1995b, 1995c, 1997a, 1997b). Key uncertainties related to inhalation risk assessment, which is the focus of this section, include the development of ECs, choice of toxicity value, lack of quantitative toxicity information via inhalation, and the approach to estimating and aggregating risks. According to EPA's *Guidance for Risk Characterization*, the discussion of uncertainty "should reflect the type and complexity of the risk assessment, with the level of effort for analysis and discussion of uncertainty

[43] For additional information on children's health risk assessment, please consult *A Framework for Assessing Health Risks of Environmental Exposures to Children* (EPA, 2006b).

corresponding to the level of effort for the assessment" (USEPA, 1995b). Therefore, risk assessors should provide a qualitative and/or quantitative evaluation of key uncertainties pertaining to inhalation risk, and their impact on the outcome of the assessment, consistent with the level of effort of the specific risk assessment.

9.2.1 Development of Exposure Concentrations

As described in Section 3 of this guidance, with the exception of acute exposures, time-weighted averages are typically used to represent intermittent or variable inhalation exposures to receptors at a site. This recommended approach is consistent with the duration adjustment approach (based on Haber's Law) that is generally used in deriving the toxicity values (see Section 2.1.1.1 for further information). As mentioned in Section 3, when evaluating situations in which the exposure is long-term, yet there are short periods of significantly higher exposure, those periods should also be assessed using appropriate short-term toxicity values. This ensures that periods of much higher exposure can be appropriately assessed and not "diluted out" in the assessment of longer-term exposure.

When information on multiple MEs exists at a site, risk assessors may choose to estimate ECs as outlined in Section 3.4. However, this typically requires sufficient time-activity information of receptors at a site to accurately determine the time spent in each ME. Incomplete or low quality data on time-activity pattern may introduce uncertainty into the estimation of the ECs for MEs. Risk assessors should describe the quality and completeness of these data.

The recommended method for determining the CA at a site can potentially introduce uncertainty into the EC calculations. For instance, if contaminant concentrations in air are measured, risk assessors should consider uncertainties related to how well the set of air samples available at a site represents the duration and time period being assessed as well as measurement uncertainty related to the methods and equipment used. In addition, risk assessors should describe any potential confounding of indoor air samples by other sources of contaminants (e.g., household products). If contaminant concentrations in air are modeled, (e.g., by EPA's spreadsheet models for vapor intrusion) risk assessors should address model-related uncertainties and their potential impact on the estimate of contaminant concentrations in air. Considerations of particle size at the site versus particle size used to derive the toxicity value are also important.

9.2.2 Toxicity Assessment

Section 4.1 of this document indicates that some IURs on IRIS were developed through extrapolation from oral CSFs (see Appendix B of this document). The use of toxicity values derived through simple route-to-route extrapolation introduces additional uncertainty into risk calculations. Therefore, risk assessors should indicate when extrapolated IURs are used and should characterize the potential impact of the uncertainty associated with using these values, if known.

Section 4.2 and Appendix C of this guidance recommends contacting STSC to help identify appropriate toxicity values for conducting a risk assessment at Superfund sites in the absence of published inhalation toxicity values. If STSC is unable to recommend a toxicity value, risk assessors should acknowledge the resulting uncertainty in risk associated with the chemical(s) lacking inhalation toxicity data. If STSC provides risk assessors with a toxicity value based on a PBPK

model, model uncertainty should be discussed. In addition, if STSC provides risk assessors with one or more structurally analogous chemicals, risk assessors can use toxicity data for these chemicals to help characterize the potential magnitude of the inhalation risk associated with the chemical(s) lacking data. In this case, risk assessors should acknowledge the uncertainty associated with relying on toxicity data for analogous chemicals to characterize risk at the site.

Risk assessors should also acknowledge chemicals that lack duration-appropriate toxicity values and discuss the potential impacts of substituting alternative toxicity values for HQ calculations. For instance, if the ED is determined to be subchronic but no subchronic inhalation RfC or analogous toxicity value is available for that chemical, the risk assessor should address the uncertainty associated with calculating an HQ using a toxicity value for a different duration, such as chronic, or the impact of not quantifying those risks. In addition, if risk assessors use an acute toxicity value that does not match the duration of the acute exposure being assessed, the possibility of under or overestimating hazard should be discussed.

When conducting a screening-level risk assessment using screening values such as those described in Section 7, it is important to further evaluate and clearly describe the quality and uncertainties associated with the inhalation toxicity values used in the risk assessment if measured sample contaminant concentrations at a site exceed these screening values.

9.2.3 Estimating Cancer Risks

For high exposures, for example those within the range of epidemiological studies (usually those predicted to have risks greater than 10^{-2}), the IUR derived from the linear extrapolation below the range of observation is generally not appropriate for use (see Section 5.1 of this document for further information).[44] Risk assessors should provide specific information in the risk characterization describing how these high exposures were addressed in the risk assessment. For instance, if a risk assessor chose to provide a semi-quantitative approach (e.g., indicating that risks are above 10^{-2}), this should be indicated, along with a description of the uncertainties involved in not fully quantifying risk associated with exposure to this chemical. If a risk assessor chose to use the original model in the IRIS file or other technical background document, the risk characterization section should include a description of any uncertainties in the model used and could contain examples of the risks estimated.

9.2.4 Estimating Risk and Hazard from Multiple Chemicals and Exposure Pathways

Risk assessors should also describe uncertainties involved in aggregating risk and hazard across multiple chemicals and exposure pathways. For instance, the approaches described in Section 8 of this document are associated with several assumptions (e.g., independence of action and doses for individual compounds at levels not expected to be of concern). If these assumptions are not met, aggregation may not be appropriate. This should be fully described in the risk characterization section and any uncertainties involved in the lack of quantitative information should be indicated.

[44] Also refer to Section 8.2.1 of *RAGS, Part A* for further discussion of this topic (EPA, 1989, page 8-6).

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APPENDICES

TABLE OF CONTENTS

LIST OF TABLES

LIST OF EQUATIONS

APPENDIX A

APPENDIX A

ANALYSIS OF DEFAULT APPROACH FOR HEC DERIVATION AS COMPARED TO POPULATION- AND LIFESTAGE-SPECIFIC CALCULATIONS

NOTE: The Agency's inhalation dosimetry methodology (USEPA, 1994; hereafter, "the *Inhalation Dosimetry Methodology"*) is a technical report that describes the derivation of human equivalent concentrations (HECs) from animal (or human) studies, as well as the other steps involved in developing a chronic Reference Concentration (RfC). This appendix is included to illustrate the HEC derivation using the *Inhalation Dosimetry Methodology*'s default approach (with the recommended default values for humans), and to also illustrate the impact of substituting alternate age- and activity-specific human values into the default calculations. The default approach is employed for chemicals for which more chemical-specific dosimetric and pharmacokinetic data are not available, thus precluding the use of more advanced models for deriving the HEC. The calculations in this appendix do not represent a refined or optimal model for assessing intra-human variability (e.g., age- and activity-specific risks), and are not intended to imply that risk assessors should deviate from the *Inhalation Dosimetry Methodology* by substituting alternate values into the default calculations. Age-specific data are limited. Because of these limitations, the calculations made for different ages and exposure groups in this appendix are not recommended for use in quantitative risk assessment (i.e., they are only for the purpose of illustration), but may be useful in discussions of uncertainty and variability associated with the default approach.

It is also noted that, as of this writing, the Agency is involved in a routine reevaluation of scientific advancements in the field, with consideration of the need for improvement to the *Inhalation Dosimetry Methodology*. Any revisions will consider current understanding of inhalation dosimetry and differences across and within species, as well as the Agency's risk assessment needs. In order to transparently and quantitatively address children's inhalation dosimetry and risk assessment, this guidance document will be updated (on-line) when Agency methodology updates are available that are specific to early life. Until that time, the 1994 *Inhalation Dosimetry Methodology* is the appropriate Agency methodology.

INTRODUCTION

This appendix consists of examples and discussions illustrating the current default chemical category-specific approach to inhalation dosimetry for the various categories of gases and particles as described in *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994; hereafter, the *Inhalation Dosimetry Methodology*). This default inhalation dosimetry approach is used to convert toxicological and epidemiological study data to an HEC that can then be used to derive chronic RfCs for the human population (inclusive of susceptible populations and life stages, such as children) and also in the development of Inhalation Unit Risks (IURs) (USEPA, 2005). The default approach does not rely on age- or activity-specific values for physiological parameters when calculating HECs; however the default approach has been designed by EPA to derive reference values that are protective across the entire population.

The appendix includes six sections. Sections 1 through 3 address Category 1 gases. These sections provide example calculations for Category 1 highly reactive, high water solubility gases that are typically absorbed in the upper airways, exhibiting adverse effects in the extrathoracic (ETh), tracheobronchial (TB), and pulmonary (PU) regions of the respiratory tract, respectively. These examples include comparisons of HEC calculations based on default parameters with those derived using age- and activity-specific parameters for the respiratory region affected. Section 4 addresses Category 3 low reactivity, limited water solubility gases that exhibit systemic effects outside the respiratory tract. Section 5 addresses changes in particle deposition in the respiratory tract across age groups. The conclusions are summarized in Section 6.

When reviewing the examples, please note the following:

- An RfC derived using the *Inhalation Dosimetry Methodology* is defined as "an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime" (USEPA, 2008).

- All examples in this appendix are based on the *Inhalation Dosimetry Methodology*. EPA is committed to periodically reviewing and updating the *Inhalation Dosimetry Methodology* to ensure that it reflects the current state of the science and that it yields toxicity values that sufficiently cover potential age- and activity-related variation in inhalation exposure. A review and update is currently underway.

- The examples in this appendix are all based on calculating HECs from a point of departure (POD) for non-cancer effects (e.g., a No Observed Adverse Effect Level (NOAEL), Lowest Observed Adverse Effect Level (LOAEL), or Benchmark Concentration, Lower confidence limit (BMCL)). These calculations could also be performed in an identical manner for carcinogens using a POD for cancer risk estimate derivation (e.g., a Lower limit on the Effective Concentration (LEC) value).

- The default animal and human values for minute volume (V_e) and surface area (SA) used in these examples were obtained from *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994).[45] The age- and activity-specific V_e values were obtained from the International Commission on Radiological Protection (ICRP) Publication 66, *Human Respiratory Tract Model for Radiological Protection* (ICRP, 1994).[46] Age-specific SA values used in Examples 1 and 2 were calculated using scaled estimates for the mass and thickness of respiratory region-specific target tissue from ICRP (1994); Values for Example 3 were calculated from an allometric scaling equation presented in a publication by Zeltner et al. (1987). EPA's Office of Research and Development (ORD) selected these data following review of the available physiological data for the age groups indicated in the examples.

- Chemical-specific data from the Integrated Risk Information System (IRIS) file for acrolein were used in the ETh example (Example 1). However, the other two examples, which focus on effects in the TB and PU regions, respectively, use hypothetical data for the POD because there are currently no chemicals on IRIS exhibiting Critical Effects (for RfC derivation) in those regions.[47] The conclusions of these two examples are unaffected by the use of hypothetical data because the results are driven by the values of parameters that are not chemical-specific (i.e., SA and V_e).

[45] The minute volume is the total ventilation per minute and equals the product of the tidal volume (the air volume entering or leaving the lungs with a single breath) and the respiratory frequency.

[46] For further information on inhalation rates in humans under different scenarios, refer to Chapter 5 of EPA's *Exposure Factors Handbook* (EPA, 1997).

[47] Hypothetical examples for the TB and PU regions were included in this appendix because currently no RfCs for gases on IRIS are calculated based on animal studies showing health effects occurring in these regions of the respiratory system

1. EXAMPLE 1: CATEGORY 1 GAS, EXTRATHORACIC EFFECTS, ACROLEIN

The Dosimetric Adjustment Factor (DAF) for a Category 1 gases, the Regional Gas Dose Ratio (RGDR), is based on the animal to human ratio of the V_e divided by the SA of the region of the respiratory tract where the effect occurs. For acrolein, the effect occurs in the ETh region. The DAF is typically calculated using the following equation (USEPA, 1994, Equation 4-18):

$$RGDR_{ETh} = \frac{\left(\frac{V_e}{SA_{ETh}}\right)_{animal}}{\left(\frac{V_e}{SA_{ETh}}\right)_{human}} = \frac{\frac{0.14\,L/min}{15\,cm^2}}{\frac{13.8\,L/min}{200\,cm^2}} = 0.14 \qquad \textbf{(Equation A-1)}$$

The default *Inhalation Dosimetry Methodology*-recommended values for the V_e and SA_{ETh} of the Wistar rat (the animal in the principal study for acrolein) are 0.14 L/min (0.20 m^3/day) and 15 cm^2, respectively (USEPA, 1994). EPA's default human values are 13.8 L/min (20 m^3/day) for V_e and 200 cm^2 for SA_{ETh} (USEPA, 1994). The RGDR for the ETh region ($RGDR_{ETh}$) was calculated using these values for the rat and the human as shown in Equation A-1. In the laboratory animal study on acrolein, the LOAEL adjusted for continuous exposure ($LOAEL_{[ADJ]}$) of 0.16 mg/m^3 (USEPA, 2003) is used as the point of departure. The $LOAEL_{[HEC]}$ is the $LOAEL_{[ADJ]}$ multiplied by the $RGDR_{ETh}$.

To illustrate any potential age- or activity-related variation in the $LOAEL_{[HEC]}$ that might result from using human parameter values other than the defaults, scaled estimates for the mass and thickness of ETh target tissue from ICRP (1994) at different ages are used to calculate the SA_{ETh} values in Table A-1. Age- and activity-related V_e reported in ICRP (1994) are based on daily time-budgeted reference values. Table A-1 shows little variation in the resultant $LOAEL_{[HEC]}$ across the groups in this example. The default procedure produces the lowest $LOAEL_{[HEC]}$ value in Table A-1 and is, therefore, sufficient to cover all of these groups.

TABLE A-1 COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE EXTRATHORACIC REGION					
	Total $V_{e\ (human)}$ (L/min)[a]	**$SA_{ETh\ (human)}$ (cm^2)[b]**	**$(V_e/SA_{ETh})_{human}$ (L/min-cm^2)**	**$RGDR_{ETh}$**	**$LOAEL_{[HEC]}$ (mg/m^3)**
Outdoor Worker, Male	17.5	470	0.037	0.25	0.04
Sedentary Worker, Male	15.4	470	0.033	0.28	0.04
Sedentary Worker, Female	12.6	407	0.031	0.30	0.05
15 Year-Old Male	14.0	439	0.032	0.29	0.05
15 Year-Old Female	10.9	397	0.027	0.35	0.06
10 Year-Old	10.6	293	0.036	0.26	0.04
5 Year-Old	6.1	198	0.031	0.30	0.05
1 Year-Old	3.6	97.1	0.037	0.25	0.04
3 Month-Old	2.0	65.8	0.030	0.31	0.05
HEC - Default	13.8	200	0.069	0.14	0.02

[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994).
[b] These values are from the ICRP publication, Tables 1 and 5 (ICRP, 1994).

2. EXAMPLE 2: CATEGORY 1 GAS, TRACHEOBRONCHIAL EFFECTS, HYPOTHETICAL CHEMICAL

The DAF for a Category 1 gas or vapor exhibiting effects in the TB region is based on the animal to human ratio of the V_e divided by the SA of the TB region for each species. The DAF is typically calculated using the following equation:

$$RGDR_{TB} = \frac{\left(\frac{V_e}{SA_{TB}}\right)_{animal}}{\left(\frac{V_e}{SA_{TB}}\right)_{human}} = \frac{\frac{0.14\ L/min}{22.5\ cm^2}}{\frac{13.8\ L/min}{3200\ cm^2}} = 1.4 \qquad \textbf{(Equation A-2)}^{48}$$

This example assumes that the hypothetical chemical has been tested on Wistar rats and therefore utilizes the EPA animal default values for that strain. The V_e value used is 0.14 L/min (0.20 m^3/day) and the default SA_{TB} is 22.5 cm^2 (USEPA, 1994). EPA's default human values are 13.8 L/min (20 m^3/day) for V_e and 3200 cm^2 for SA_{TB} (USEPA, 1994). The RGDR for the TB region ($RGDR_{TB}$) is calculated using these values for the rat and the human, as shown in Equation A-2. The example also assumes a NOAEL adjusted for continuous exposure ($NOAEL_{[ADJ]}$) of 0.16 mg/m^3 as the point of departure. The $NOAEL_{[HEC]}$ is the $NOAEL_{[ADJ]}$ multiplied by the $RGDR_{TB}$.

Table A-2 shows little variation across age and activity groups in the $NOAEL_{[HEC]}$. The variation from the default (less than a factor of 2) is less than the default value of 10 used for the uncertainty factor for intraspecies variability when deriving the RfC. Application of the normal procedure for

[48] This equation is the reduced, default version of Equation 4-19 of the *Inhalation Dosimetry Methodology*. Equation 4-19 is reduced to this form consistent with the derivation of the reduced form of the RGDR equation of extrathoracic effects described in section 4.3.6.1 and Appendix I of the *Inhalation Dosimetry Methodology*.

determining the RfC will accommodate the observed variation. In addition, RfCs and IURs are developed for chronic exposure and will generally involve an exposure for multiple years.

TABLE A-2
COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE TRACHEOBRONCHIAL REGION

	Total $V_{e\ (human)}$ (L/min)[a]	$SA_{TB\ (human)}$ (cm^2)[b]	$(V_e/SA_{TB})_{human}$ (L/min-cm^2)	$RGDR_{TB}$	$NOAEL_{[HEC]}$ (mg/m^3)
Outdoor Worker M	17.5	2660	0.0066	0.94	0.15
Sedentary Worker M	15.4	2660	0.0058	1.1	0.18
Sedentary Worker F	12.6	2640	0.0048	1.3	0.21
15 year M	14.0	2520	0.0056	1.1	0.18
15 year F	10.9	2250	0.0048	1.3	0.21
10 Year	10.6	1830	0.0058	1.1	0.18
5 Year	6.1	1340	0.0046	1.4	0.22
1 Year	3.6	857	0.0042	1.5	0.24
3 Months	2.0	712	0.0028	2.2	0.35
HEC-default	13.8	3200	0.0043	1.4	0.22

[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994).
[b] These values are from the ICRP publication, Tables 1 and 5 (ICRP, 1994).

3. EXAMPLE 3: CATEGORY 1 GAS, PULMONARY EFFECTS, HYPOTHETICAL CHEMICAL

The DAF for a Category 1 gas or vapor with an effect in the PU region is based on the animal to human ratio of the alveolar ventilation rate (Q-alv) divided by the SA of the PU region (SA_{PU}) for each species. The Q-alv is approximately equal to the V_e multiplied by 0.7. This adjustment accounts for the anatomic/physiologic deadspace in the PU region, making the Q-alv equivalent to the amount of inspired air available for gas exchange (West, 2000). The DAF for this region of the respiratory tract is typically calculated using the following equation:

$$RGDR_{PU} = \frac{\left(\frac{Q-alv}{SA_{PU}}\right)_{animal}}{\left(\frac{Q-alv}{SA_{PU}}\right)_{human}} = \frac{\frac{0.1\,L/min}{0.34\,m^2}}{\frac{9.7\,L/min}{54\,m^2}} = 1.6 \qquad \textbf{(Equation A-3)}^{49}$$

This example assumes that the hypothetical chemical has been tested on Wistar rats and therefore utilizes the EPA animal default values for that strain. The V_e valued used is 0.14 L/min (0.20 m^3/day), which when multiplied by 0.7, yields a Q-alv of 0.1 L/min. The example uses the EPA default rat SA_{PU} of 0.34 m^2 (USEPA, 1994). EPA's default human values are 13.8 L/min (20

[49] This equation is the reduced, default version of Equation 4-23 of the *Inhalation Dosimetry Methodology*. Equation 4-23 is reduced to this form consistent with the derivation of the reduced form of the RGDR equation of extrathoracic effects described in section 4.3.6.1 and Appendix I of the *Inhalation Dosimetry Methodology*.

m^3/day) for V_e (which yields a Q-alv of 9.7 L/min) and 54 m^2 for SA_{PU} (USEPA, 1994). The RGDR for the PU region ($RGDR_{PU}$) is calculated using these values for the rat and the human, as shown in Equation A-3. The example also assumes a $NOAEL_{[ADJ]}$ of 0.16 mg/m^3 as the point of departure. The $NOAEL_{[HEC]}$ is the $NOAEL_{[ADJ]}$ multiplied by the $RGDR_{PU}$.

Table A-3 below provides the Q-alv values for humans based on the daily time-budgeted V_e for different ages and activity levels from the ICRP publication (1994). SA data for the PU region in the ICRP publication are estimated using an allometric scaling model fitted to data from a morphometric analysis of SA_{PU} in a sample of seven children (ranging in age from 26 days to 5 years) and eight adults (Zeltner et al., 1987). ORD selected the Zeltner analysis for this example because these SA_{PU} data are based on empirical morphometric measurements of human lungs as opposed to scaled estimates determined from lung models (such as those done by Yu and Xu, 1987 or Yu and Yoon, 1991). In addition, the children and adult SA_{PU} values calculated in the Zeltner analysis are supported by several independent studies that measured SA_{PU} in children (Langston et al., 1984) or in adults using similar morphometric techniques (Crapo et al., 1982 & 1983; Stone et al., 1992; Mercer et al., 1994).

Table A-3 shows little variation in the resultant $NOAEL_{[HEC]}$ across the groups in this example. The default procedure produces the lowest $NOAEL_{[HEC]}$ value in Table A-3 and is, therefore, sufficient to cover all of these groups.

TABLE A-3

COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE PULMONARY REGION

	Total V_e (L/min)[a]	$Q\text{-}alv_{(human)}$ (L/min)[b]	$SA_{PU\ (human)}$ (m^2)	$(Q\text{-}alv/SA_{PU})_{human}$ (L/min-m^2)	$RGDR_{PU}$	$NOAEL_{HEC}$ (mg/m^3)
Outdoor Worker, Male	17.5	12	139	0.088	3.3	0.53
Sedentary Worker, Male	15.4	11	139	0.078	3.7	0.59
Sedentary Worker, Female	12.6	8.8	114	0.077	3.8	0.61
15 Year-Old Male	14.0	9.8	108	0.091	3.2	0.51
15 Year-Old Female	10.9	7.6	100	0.076	3.8	0.61
10 Year-Old	10.6	7.4	62.0	0.12	2.4	0.38
5 Year-Old	6.1	4.3	37.3	0.11	2.6	0.42
1 Year-Old	3.6	2.5	18.5	0.14	2.1	0.34
3 Month-Old	2.0	1.4	11.0	0.13	2.2	0.35
HEC-Default	13.8	9.7	54.0	0.18	1.6	0.26

[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994).
[b] These values are from Zeltner et al. (1987).

4. CATEGORY 3 GASES

The DAF for a Category 3 gas or vapor is based on the ratio of the animal blood:gas partition coefficient to the human blood:gas partition coefficient and is typically calculated using the following equation:

$$DAF = \frac{(H_{b/g})_{animal}}{(H_{b/g})_{human}} \qquad \textbf{(Equation A-4)}$$

The blood:gas partition coefficient is primarily determined by the solubility of the gas in an aqueous medium as well as the protein and lipid content of the blood. There is little reason to suspect that the blood:gas partition coefficient for a non-metabolized chemical will vary greatly across the human population. The limited data available indicate no difference in the blood:gas partition coefficient with age for methylene chloride in mice (Thomas et al., 1996), and for sevoflurane, isoflurane, and halothane in humans (Malviya and Lerman, 1990). Two studies examining the solubility of volatile anesthetics (isoflurane, enflurane, halothane, and methoxyflurane) in the blood and body tissues found higher blood:gas partition coefficients in adults compared with children (Lerman, et al., 1984 & 1986). Any variability in the blood:gas partition coefficient with age is expected to be less than the default value of 10 used for the uncertainty factor for intraspecies variability when deriving the RfC. Any variability in the blood:gas partition coefficient with age is also not expected to cause a large overestimate or underestimate in the calculated cancer risk.

Because of the limited data available, the *Inhalation Dosimetry Methodology* makes the science policy decision to use a value of one for the ratio of the partition coefficients when the animal to human ratio exceeds one or when the animal or human value is unknown. At this time, all chemicals on IRIS for which both human and animal data are available have an animal to human ratio of partition coefficient greater than 1.[50] Therefore, the default assumption of one is a conservative approach that is not likely to underestimate the chemical-specific DAF.

5. PARTICLE DEPOSITION ACROSS AGE GROUPS

The DAF for a particle causing an effect in the respiratory tract, the Regional Dose Deposition Ratio ($RDDR_r$), is based on the animal to human ratio of the V_e and the fractional deposition of the particle in that region (F_r), divided by the surface area of the region where the effect occurs (SA_r) (USEPA, 1994). Inherent in this derivation is the assumption that 100 percent of the deposited dose remains in the respiratory tract and any clearance mechanisms are not considered. The $RDDR_r$ is typically calculated using the following equation:

$$RDDR_r = \frac{\left(\frac{V_e}{SA_r} \times F_r\right)_{animal}}{\left(\frac{V_e}{SA_r} \times F_r\right)_{human}} \qquad \textbf{(Equation A-5)}$$

[50] While 1,4-dioxane has not yet been evaluated on IRIS, it provides an exception to this statement, in that the blood:gas partition coefficient is 2750 for mice, 1850 for rats, and 3650 for humans, yielding an animal to human ratio of 0.75 for mice and 0.51 for rats (Reitz et al., 1990).

The DAF for a particle causing an extra-respiratory (ER) effect, the $RDDR_{ER}$, is based on the animal to human ratio of the V_e and the total deposition of the particle in the entire respiratory tract (F_{total}), divided by body weight (BW) (USEPA, 1994). The $RDDR_{ER}$ assumes that 100 percent of the deposited dose in the entire respiratory tract is available for uptake into the systemic circulation. The following general equation can be used to estimate the $RDDR_{ER}$:

$$RDDR_{ER} = \frac{\left(\frac{V_e}{BW} \times F_{total}\right)_{animal}}{\left(\frac{V_e}{BW} \times F_{total}\right)_{human}} \qquad \textbf{(Equation A-6)}$$

The information on particle deposition in various age groups is quite limited. A discussion of the current state of the science can be found in the *Air Quality Criteria for Particulate Matter Volume II*, Section 6.2.3.2 (USEPA, 2004; hereafter, *PM Criteria Document*).

Experimental and modeling results are summarized in Table A-4. The results for experimental studies are mixed, some suggesting higher deposition in children and others finding no difference across age groups. Bennett and Zeman (1998) and Schiller-Scotland et al. (1994) found no difference between total deposition of particles in the respiratory tract of children (aged 7 to14 and 6 to12, respectively) and adults for 1 to 2 micrometer particles. Schiller-Scotland et al. did find two- to three-fold higher total particulate deposition in 6 to 12 year olds for particles of 2 to 3 micrometers in size. In addition, Bennett et al. (1997) found that deposition in the ETh region was 50 percent greater in children than adults. The *PM Criteria Document* concludes that "these...studies ...do not provide unequivocal evidence for significant differences in deposition between adults and children" (USEPA, 2004, page 6-29). The document notes, however, that children may have higher activity levels and higher associated minute ventilation per lung size, potentially causing a greater size-specific dose of particles to the lung.

Modeled results suggest a higher deposition of particles in the TB region of children when compared to adults, depending on the particle size (Xu and Yu (1986); Hofmann et al. (1989); Musante and Martonen (1999); Phalen and Oldham (2001); Asgharian et al. (2004); Jarabek et al. (2005); Ginsberg et al. (2005)). Mixed results again are found in modeling studies for total deposition and deposition in other respiratory regions. In general, where differences are observed in either experimental or modeled studies, variability in deposition between age groups has been reported to be most often in the range of 1- to 3-fold greater for children than for adults, but ranging from equivalency or less up to 7-fold greater.[51]

[51] A modeling analysis examining deposition fraction per unit area at various airway generations of the lung as a function of age for various particle sizes (ranging from 0.01 to 10 μm) reported comparisons between a 3-month old and 21-year old that ranged from equivalency up to a 14-fold difference in this metric for some specific airway generations (Asgharian et al., 2004).

TABLE A-4
PARTICLE DEPOSITION ACROSS AGE GROUPS

Study	Particle Size	Results
Experimental Studies		
Becquemin et al. (1991)	Various	Nasal deposition higher in adults (up to 1.8-fold higher at rest and up to 3.4-fold higher during exercise) than children – meaning that thoracic airways of children are less protected than those of adults.
Bennett et al. (1997)	4.5 µm	-ETh deposition of particles 50 percent greater in children (higher for younger ages). -No significant difference in total respiratory tract deposition.
Bennett and Zeman (1998)	1-2 µm	No difference between 7-14 year olds and adults in total deposition of particles in the respiratory tract.
Schiller-Scotland et al. (1994)	1-2 µm	No difference between 6-12 year olds and adults in total deposition of particles in the respiratory tract.
	2-3 µm	Two- to three-fold higher total deposition of particles in 6-12 year olds versus adults.
Modeled Studies		
Asgharian et al. (2004)	0.01-10 µm	-Up to 1.2-fold higher total deposition in 3 month olds compared to adults in the TB region. -Up to 1.5-fold higher total deposition in 8 year olds compared to adults in the alveolar region. Total deposition higher in adults than 3 and 23 month olds (up to 2-fold). -Estimates of deposition fraction per unit area at various airway generations of the lung and various particle sizes highest for 3 month olds compared to adults (up to 14-fold). Higher deposition also seen for 23 month olds (up to 5-fold) and 8 year olds (up to 3-fold) compared with adults. No difference in deposition in 14 year olds compared to adults.
Cheng et al. (1995)	0.0046-0.2 µm	Nasal casts of children's airways found increased deposition efficiency for ultrafine particles with decreasing age, suggesting that young children may receive a higher dose of ultrafine particles to the upper airways.
Ginsberg et al. (2005)	0.001-10 µm	-Higher deposition in 3 month olds compared with adults for coarse and fine particles in the upper TB (up to 2-fold) and PU (up to 4-fold) regions. -Higher deposition in adults in the lower TB region.
Hoffmann et al. (1989)	1-2 µm	-1.5- to 2-fold higher total deposition in the TB region for particles in resting 8 year olds versus adults. -40-50 percent lower total deposition of particles in 8 year olds under conditions of exercise.
Jarabek et al. (2005)	0.3-6 µm	-Retained mass in the TB region normalized to regional SA was compared across age groups. -Up to 2-fold lower deposition in 3 month olds compared to adults. -Up to 2-fold higher deposition in 3 year olds and 14 year olds compared to adults.
Musante and Martonen (1999)	0.25-5 µm	-Total deposition was generally higher in children (ages 7, 22, 48, and 98 months) than adults (e.g., total lung deposition in 48-month olds was 38 percent higher than adults for 1µm particles). -TB deposition monotonically decreased as a function of age (i.e., younger children had increased TB deposition). -PU deposition greatest in the 48 and 98-month children.
Musante and Martonen (2000)	2 µm	3-fold higher deposition of particles in the PU region for 7 month olds versus adults.
Oldham et al. (1997)	Various	Airway models of trachea and bronchial airways showed total deposition in children (ages 4 and 7) greater than adult (up to approximately 7-fold higher for 4 year olds compared to adults for 4.5 µm particles).
Phalen and Oldham (2001)	0.1-10 µm	-No difference in total deposition of particles in 2 year olds versus adults. -Somewhat higher (13-81 percent; depending on particle size) deposition of particles in the TB region. -Lower deposition of particles in the PU region.
Xu and Yu (1986)	Various	Increased total deposition (up to 1.5-fold higher) in children aged 6 months, 2 years, and 8 years compared with adults for particles of varying sizes.

6. CONCLUSIONS

The examples and discussions included in this appendix suggest that the *Inhalation Dosimetry Methodology's* default approaches for derivation of the HEC for Category 1 gases with effects in the ETh, TB, and PU regions and for Category 3 gases typically are sufficient to cover variation across human age- and activity-level groups. The process for deriving an RfC from the HEC includes applying an uncertainty factor (UF) to account for within-species variability, adding further protection. When deriving an IUR for a carcinogen, UFs are not used. However the procedures for estimating an IUR incorporate conservative assumptions that would likely accommodate the degree of variation observed in these examples.

Experimental and modeling results for particles suggest the potential for small differences in deposition of particles in the respiratory tract as a function of age. The assumption that 100 percent of the deposited dose is available for uptake into the systemic circulation (for remote acting toxicants), or for activity in the respiratory tract (for local toxicity) is likely to result in an overestimation of dose to the target tissue. Any small variation in deposition among age groups should be considered against the potential magnitude of such overestimation. These differences in calculated deposition are small relative to the default 10-fold UF that accounts for intra-species variability in the derivation of the RfC. In addition, RfCs and IURs are developed for chronic exposure and will generally involve an exposure for multiple years. No additional correction of the toxicity values for these age groups is needed when the RfC or IUR is used in a risk assessment. Calculations in these examples are based on empirical data from sources listed and referenced in ICRP Publication 66 (ICRP, 1994). While ORD selected the ICRP values as the best estimates for these examples, other published values for V_e and SA exist. The use of alternate values may change the $LOAEL_{[HEC]}$ calculated for the various populations and life stages and may show more or less variability in results across the age and activity groups. In addition, the examples for the TB and PU regions are based on a hypothetical chemical, since currently no RfCs for gases on IRIS are calculated based on animal studies showing health effects occurring in these regions of the respiratory system. Given the parameter values used in the default method for calculating the HEC, it is likely that the process would yield results sufficient to cover populations and life stages with varying activities and physiologic characteristics.

Note that the available data, albeit limited, generally support these conclusions. As recommended by the Reference Dose (RfD)/RfC Technical Panel (USEPA, 2002), EPA has been exploring issues involving dose to the young from inhalation exposures, both theoretically and experimentally as well as further considering the existing animal-to-human extrapolation procedures described in current methodologies (e.g., USEPA, 1994). This is especially important because of the significant developmental changes that occur in the lung from birth well into adolescence (Pinkerton and Joad, 2000). The review and updating of these methodologies will be based on the best available science.

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APPENDIX B

APPENDIX B

CHEMICALS ON IRIS WITH EXTRAPOLATED INHALATION UNIT RISKS

Table B-1 contains chemicals on the Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS) with Inhalation Unit Risk (IUR) values calculated by extrapolation using the default ventilation rate and body weight from the oral Cancer Slope Factor (CSF). These chemicals cause tumors remote from the respiratory tract. Also listed is the year EPA verified the cancer assessment. The list was compiled in September 2008.

EPA recommends that extrapolated IURs should be used with risk Equations 6 and 11 in the main document without additional modification for calculation of cancer risk by the inhalation route of exposure. It is generally not appropriate to make adjustments based on ventilation rate and body weight using the intake equation, because the amount of the chemical that reaches the target site of the chemical through the inhalation pathway is not a simple function of the inhalation rate and body weight. Risk assessors should outline the uncertainties involved in using extrapolated IURs in the risk characterization section of the risk assessment.

TABLE B-1 CHEMICALS WITH EXTRAPOLATED INHALATION UNIT RISKS ON IRIS	
Chemical	**Year of Verification**
Acrylamide[1]	1988
Aldrin	1987
Aramite	1991
Azobenzene	1988
Bromoform	1989
Chlordane	1997
Chloroform[1]	1987
DDT	1987
1,2-Dichloroethane	1986
Dieldrin	1987
1,2-Diphenylhydrazine	1986
Heptachlor	1987
Heptachlor epoxide	1987
Hexachlorobenzene	1989
Hexachlorobutadiene[1]	1986
Alpha-hexachlorocyclohexane	1986
Beta-hexachlorocyclohexane	1986
Technical-hexachlorocyclohexane	1986
Hexachlorodibenzo-p-dioxin mixture	1987
Hexachloroethane	1986
N-nitroso-di-n-butylamine	1986
N-nitrosodiethylamine	1986
N-nitrosodimethylamine	1986
N-nitrosopyrrolidine	1986
Polychlorinated biphenyls	1996
1,1,2,2-Tetrachloroethane	1986
1,1,1,2-Tetrachloroethane	1988
Toxaphene	1987
1,1,2-Trichloroethane	1986
2,4,6-Trichlorophenol	1989
[1] Note that this chemical's IUR is currently under review.	

APPENDIX C

APPENDIX C

STSC's PROCESS FOR DERIVING ALTERNATIVE INHALATION TOXICITY VALUES

If Reference Concentration (RfC) and/or Inhalation Unit Risk (IUR) values for an inhaled contaminant are not available from the sources in the Environmental Protection Agency's (EPA's) Office of Solid Waste and Emergency Response (OSWER) hierarchy, risk assessors should first contact the National Center for Environmental Assessment's (NCEA's) Superfund Health Risk Technical Support Center (STSC) for guidance.[52] Risk assessors working on Superfund sites can contact STSC to determine whether a provisional peer-reviewed toxicity value (PPRTV) exists for a contaminant; if not, the risk assessor, in cooperation with the appropriate EPA Regional office may request that STSC develop a PPRTV document or that STSC develop an inhalation toxicity value as a "consult." The latter would be specific to the site in question only.

As a first choice, if human or whole animal studies exist providing a suitable No Observable Adverse Effect Level (NOAEL)/Lowest Observable Adverse Effect Level (LOAEL) or Point of Departure (POD) from a Benchmark Dose (BMD) analysis, this data normally will be used by STSC to develop an inhalation toxicity value. If, in addition, a suitable human inhalation physiologically based pharmacokinetic (PBPK) model exists that can be utilized to refine the dose metric to the target organ, then this information generally will be included in developing an inhalation toxicity value.

If no appropriate whole animal or human studies exist, but an appropriate peer reviewed human inhalation PBPK model exists that has been validated by experimental results, then STSC usually will attempt to derive an inhalation toxicity value from this model. If none exists, but a suitable PBPK animal inhalation models exists, STSC may attempt developing a human model and deriving an inhalation value.

PBPK modeling quantitatively describes the absorption/metabolism/distribution and elimination of the chemical from a point of entry (oral, inhalation, dermal) to the target organ(s). In some cases, an oral PBPK model can be extrapolated to the inhalation pathway, but care must be taken to consider direct pulmonary effects that may not be evident by oral dosing.

As a next approach, STSC typically will evaluate development of an inhalation toxicity value using a suitable surrogate chemical based on a quantitative structure-activity relationship (QSAR) model with structural selection criteria and solubility/toxicity considerations. STSC may evaluate possible surrogate chemicals based on several available structural models and provide a comparison. Selection of the appropriate surrogate may depend on the weight of evidence of these models.

[52] All contact with STSC should be performed by an EPA regional risk assessor. States and other entities should first contact their EPA regional risk assessor with questions on inhalation toxicity values. Regional risk assessors can then contact STSC on their behalf.

If STSC uses any of the methods for developing toxicity values other than from human or whole animal data, the value normally will be presented as a "screening" value with the caveat that it should not be used as a risk driver for a site without consultation with the STSC. The uncertainties associated with using toxicity values derived through PBPK modeling or QSAR, or with using a surrogate value should be described in the risk characterization portion of the risk assessment (see Section 9). Risk assessors are discouraged from performing simplistic route-to-route extrapolations from oral data using default assumptions about Inhalation Rate (IR) and body weight (BW).[53]

[53] If STSC indicates that no quantitative toxicity information for the inhalation route is available, the risk assessor should conduct a qualitative evaluation of this exposure route. The risk assessor should discuss in the uncertainty section of the risk assessment report the implications of not quantitatively assessing risks due to inhalation exposures to chemicals lacking inhalation toxicity data. See the section on Risk Characterization (Section 9) in the main text of this guidance for more information.

Exhibit F

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FEDERAL CONTAMINATED SITES RISK ASSESSMENT IN CANADA

Interim Guidance on

Human Health Risk Assessment for Short-Term Exposure to Carcinogens at Contaminated Sites

2013
Prepared by:
Contaminated Sites Division
Safe Environments Directorate

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

PREFACE

The Federal Contaminated Sites Action Plan (FCSAP) is a program of the Government of Canada designed to achieve improved and continuing federal environmental stewardship as it relates to contaminated sites located on federally owned or operated properties. Guidance documents on human health risk assessment (HHRA) prepared by the Contaminated Sites Division of Health Canada in support of the FCSAP are available on our website and may also be obtained by contacting the Contaminated Sites Division at *cs-sc@hc-sc.gc.ca*.

This interim guidance document provides additional direction for custodial departments with respect to amortization of short-term exposure to carcinogens at contaminated sites. It is of particular importance at remote sites or sites that are accessed infrequently. The guidance is intended to be advisory in nature and will be updated periodically on the basis of revisions to current expertise, applicable standards and recommendations received from stakeholders. Readers are advised to consult with Health Canada, Contaminated Sites Division, to confirm that they are using the most recent version available on the Health Canada website and that the use of HHRAs is reflective of current and best practices. This document is not to be considered a substitute for the guidance of a qualified professional practitioner.

Work and opinions from various consultants, academics and governmental agencies were used to create this guidance. In particular, Angela Li-Muller, Margaret Yole, Norm Healey and Sanya Petrovic of Health Canada are recognized for their contribution.

Health Canada requests that any questions, comments, criticisms, suggested additions or revisions to the document be directed to the following: Contaminated Sites Division, Safe Environments Directorate, Health Canada, 269 Laurier Avenue West, 4th floor, Address Locator: 4904A, Ottawa, ON K1A 0K9. Email: *cs-sc@hc-sc.gc.ca*.

See also: *www.hc-sc.gc.ca/ewh-semt/contamsite/index-eng.php*.

ABBREVIATIONS AND ACRONYMS

A-D	Armitage-Doll
ADAF	age-dependent adjustment factors
AF	absorption factor
ASF	age sensitivity factor
BHT	butylated hydroxytoluene
BW	body weight
C	concentration
CalEPA	California Environmental Protection Agency
CSD	Contaminated Site Division
DES	diethylstibesterol
DMBA	dimethylbenzanthracene
DNA	deoxyribonucleic acid
DQRA	detailed quantitative risk assessment
ED	exposure duration
ED_{01}	maximum likelihood estimate of the dose corresponding to a 1% additional cancer risk
ER	exposure rate
FCSAP	Federal Contaminated Sites Action Plan
HC	Health Canada
HHRA	human health risk assessment
ILCR	incremental lifetime cancer risk
IR	intake rate
LADD	lifetime average daily dose
LMS	linearized multistage
LOAEL	lowest observed adverse effect level
MVK	Moolgavkar-Venzon-Knudson
NOAEL	no observed adverse effect level
PAHs	polycyclic aromatic hydrocarbons
PBBs	polybrominated biphenyls
PBPK	physiologically based pharmacokinetic
PQRA	preliminary quantitative risk assessment
SF	slope factor
TC	tolerable concentration
TDI	tolerable daily intake
TRV	toxicological reference value
UR	unit risk
US EPA	United States Environmental Protection Agency

EXECUTIVE SUMMARY

This document provides guidance for application at federal contaminated sites funded under the Federal Contaminated Sites Action Plan (FCSAP). It is considered to be interim and is based on an assessment of the current scientific literature. The document does not represent the opinion of Health Canada outside the application of federal contaminated sites funded under the FCSAP.

The current approach to evaluating health risks associated with human exposure to carcinogens at contaminated sites focuses on incremental lifetime cancer risks. The approach to cancer risk assessment varies according to the mode of action at the tumour site in question. Unless there is evidence to support a threshold mode of action, the current approach assumes a linear dose-response relationship at low doses (i.e. non-threshold). The incremental lifetime cancer risk (ILCR) is calculated as a product of the lifetime daily dose (or concentration) and the toxicological reference value (TRV), expressed as cancer slope factor (or inhalation unit risk).

A threshold approach can be applied when there are sufficient data to ascertain the mode of action at the tumour site in question and to conclude that the dose-response relationship is not linear at low doses. For these carcinogenic effects, the TRVs are expressed as tolerable daily intakes (TDIs) or concentrations (TCs), the intakes or concentrations to which it is believed that a person can be exposed daily over a lifetime without deleterious effects. Human exposure is compared with these TRVs, where appropriate, to determine health risks.

Characterization of human cancer risks usually makes use of TRVs that have been derived from epidemiological or toxicological studies with comparable exposure patterns. TRVs for carcinogens are often based on the results of animal studies in which the animals were exposed on a daily basis throughout their adult lifespan. Exposures at contaminated sites may mirror these exposure patterns, but in some circumstances exposures may occur over a period of time much shorter than the lifetime of the exposed individual. In a short-term exposure scenario, short-term exceedance (or excursion) above chronic average daily exposure could occur as a result of variation in intake rates or daily fluctuation in chemical concentrations in environmental media. As a result, the health risks of short-term exposure often need to be addressed.

For contaminated site risk assessments, the current practice of characterizing ILCR associated with less-than-lifetime exposures to carcinogens that act via a non-threshold mode of action involves averaging the short period of exposure over a lifetime to calculate the lifetime average daily dose (LADD). Several issues regarding this practice of averaging the exposure have been raised:

- There is a potential for underestimating cancer risks with the practice of time-averaging of exposures (LADD).
- Variability in sensitivity among different lifestages may not be fully considered.

In addition, depending on the magnitude of exposure, carcinogenic agents may elicit other, chronic and short-term non-cancer health effects as a result of short-term exposures. At present, these effects are often not evaluated.

The Contaminated Sites Division (CSD) will continue to review information related to risk assessments for carcinogenic agents, including short-term exposure and dose averaging.

Cancer Risk Assessment: Non-Threshold Carcinogenic Effects

A literature review was conducted to evaluate whether averaging short-term exposure over a lifetime would be adequate to estimate cancer risk using cancer slope factors derived from chronic animal studies. Both theoretical studies using mathematical models of carcinogenesis and empirical studies involving exposure during discrete age windows suggest that exposures in early lifestages are usually associated with a higher risk of carcinogens acting through a mutagenic mode of action. It was concluded that application of age-dependent adjustment factors to the cancer slope factor with exposure averaged over a lifetime can provide a generally conservative estimate of lifetime cancer risks. As an interim measure, the United States Environmental Protection Agency (EPA) approach has been adopted as a default recommendation for contaminated site risk assessments.

The ILCR can be estimated by summing the risk from each discrete exposure period. For non-threshold carcinogens acting through a mutagenic mode of action, it is recommended that age-dependent adjustment factors (ADAFs) be applied to the cancer slope factor (or inhalation unit risk) with exposure averaged over a lifetime to account for the sensitivity of the age-specific exposure period. We have developed default ADAFs by adjusting the US EPA's ADAFs to be consistent with the age groups recommended by CSD. These default factors can be applied when age-specific cancer slope factors (or inhalation unit risks) or chemical-specific data are not available.

When exposure periods do not match the CSD's age groupings, CSD recommends that the US EPA's ADAFs be applied. For example, if exposure occurs only between 7 months and less than 2 years of age, the adjustment factor of 10 applies. Likewise, if exposure occurs only between 12 and < 16 years of age, the ADAF of 3 applies. When chemical-specific data are available for a susceptible lifestage, these data can be used directly to evaluate risks for the chemical and the lifestage on a case-by-case basis.

Recommended interim adjusted age-dependent adjustment factors (ADAFs) for cancer risk assessment at contaminated sites for carcinogenic effects via a mutagenic mode of action

Lifestage	Age	Adjusted age-dependent adjustment factor (ADAF)[a]
Infant	0–6 months	10
Toddler	7 months–4 years	5[b]
Child	5–11 years	3
Teenager	12–19 years	2[c]
Adult	20+	1

[a] US EPA (2005 a, b), except as noted.

[b] $ADAF_{7\ mo-4\ yr} = (ADAF_{0-<2} * D_{7\ mo-1} / D_{7\ mo-4}) + (ADAF_{2-4} * D_{2-4} / D_{7\ mo-4}) = 10 * 1.5/4.5 + 3 * 3/4.5 = 5$, and D_i = exposure duration in years

[c] $ADAF_{12-19} = (ADAF_{12-<16} * D_{12-15} / D_{12-19}) + (ADAF_{16+} * D_{16-19} / D_{12-19}) = 3 * 4/8 + 1 * 4/8 = 2$, and D_i = exposure duration in years

When the mode of action is unknown or the burden of proof for a threshold mode of action has not been met, CSD recommends a non-threshold approach to cancer risk estimation. If chemical-specific data are available on quantitative differences between early lifestages and adults, an analysis of the differences could be used to adjust risk estimates for early life exposures. Otherwise, CSD does not recommend extending the default age-dependent potency adjustment factors to these carcinogenic effects. This position would be analogous to recommending a default ADAF of 1 for all lifestages.

Cancer Risk Assessment: Threshold Carcinogenic Effects

At this time, the CSD does not recommend a default age-specific adjustment for carcinogenic effects determined to have a non-linear dose-response relationship (i.e. threshold) at low doses. Adjustment can be made on a chemical-specific basis if supported by experimental data. These substances would be included in an HHRA using a TDI (or a TC in the case of inhalation exposure).

The CSD recommends that dose averaging for short-term exposure for these types of carcinogenic effects be performed in the same way as for substances with threshold non-carcinogenic effects. It is important that dose averaging should not underestimate the potential for threshold carcinogenic effects. Without a sound basis for doing so (i.e. it cannot be a default assumption), the human health risk assessor should not simply mathematically spread out a short-term dose over a longer period and conclude that the short-term dose is toxicologically equivalent to a lower dose over the long period. Instead, exposure should be averaged over the total actual exposure period and compared with the appropriate TRV. A scientific rationale is required to support any proposed amortization (dose averaging beyond actual exposure period) to ensure that short-term risks are not underestimated. This analysis needs to be done on a chemical-specific basis.

Assessment of Potential Non-Cancer Health Effects from Short-Term Exposure

For short-term exposure, carcinogenic agents may elicit other, chronic and short-term non-cancer health effects, depending on the magnitude of exposure. Short-term effects can be evaluated for potential critical receptors/lifestages[1] using short-term TRVs where available (either from other regulatory agencies or derived from literature values as per the Health Canada, 2010, detailed quantitative risk assessment [DQRA] guidance) and when applicable to the exposure scenarios. If short-term TRVs are not available, such evaluation can be conducted on the basis of relevant dose-response information from toxicity studies. It is also important to consider whether the short-term exposure might elicit early biological key events that might progress to health effects at a later date.

[1] Including relevant receptors/lifestages with the highest exposure and receptors/lifestages associated with specific sensitivity to the toxicity of the contaminants.

1.0 INTRODUCTION

1.1 Current Cancer Risk Assessment Approach

Health Canada's Contaminated Sites Division (CSD) has a current risk assessment approach for carcinogenic effects that assumes a linear dose-response relationship at low doses (non-threshold) unless there are adequate data to ascertain a mode of action that is consistent with a non-linear dose-response relationship at low doses (i.e. threshold). This approach is particularly relevant for agents that are mutagenic[2] and DNA reactive. The incremental lifetime cancer risk is calculated as a product of the lifetime daily dose and cancer slope factor.

A threshold approach can be applied when there are sufficient data to ascertain the mode of action at the tumour site in question and to conclude that the dose-response relationship is not linear at low doses. Such a carcinogenic agent usually has not been shown to demonstrate mutagenic or other properties consistent with linearity at low doses. Endocrine disruption, cell proliferation, cytotoxicity and receptor-binding are some examples of a non-linear mode of action. For these carcinogenic effects, the CSD risk assessment approach assumes a non-linear dose-response relationship at low doses. The toxicological reference value (TRV) is derived by applying an uncertainty factor to a benchmark dose or benchmark concentration (if available)—a NOAEL (no observed adverse effect level) or a LOAEL (lowest observed adverse effect level)—as appropriate to establish a tolerable daily intake (TDI) or concentration (TC), i.e. the intake or concentration to which it is believed that a person can be exposed daily over a lifetime without deleterious effects.

In many cases, non-carcinogenic effects rather than carcinogenicity may be the main determinant of health risk from long-term exposure to the threshold carcinogenic agent. For example, the developmental effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin occur at lower exposure levels than those required for carcinogenicity and have been used to establish the TRV.

1.2 Issues Related to Less-Than-Lifetime Exposure to Carcinogens at Contaminated Sites

Short-term exposure to carcinogens at contaminated sites may be associated with activities that occur over a relatively short period of time, such as seasonal activities like camping, occasional visits to a remote site and certain occupational activities, e.g. construction and underground service installation. As a result, short-term health risks need to be addressed.

The significance of exposure to contaminants is best characterized by comparison with TRVs derived from epidemiological or toxicological studies with comparable exposure patterns (i.e. short-term exposure compared with TRVs derived from a short-term study). Otherwise, significant uncertainty could be introduced into risk characterization.

TRVs for carcinogens are often based on the results of animal studies in which the animals were exposed on a daily basis throughout their adult lifespan. Exposures to human receptors at a contaminated site may mirror this pattern of exposure, but more often exposure occurs for only a portion of the lifetime or may be intermittent. Exposures at a contaminated site may occur during childhood or in utero, lifestages not represented in standard cancer bioassays.

The current practice of characterizing incremental lifetime cancer risks (ILCR) associated with less-than-lifetime exposures to non-threshold carcinogens involves averaging the short period of exposure over a lifetime to calculate the lifetime average daily dose (LADD). The following issues related to dose averaging (sometimes referred to as dose amortization) have been raised when exposures occur over a short time frame:

1. There is a potential for underestimating cancer risks with the calculation of a LADD associated with a short exposure period.
2. The possibility of acute/subchronic non-cancer effects due to elevated exposures has not been considered and may be relevant when the exposure is elevated above the LADD over a subchronic period. For example, the physiological response will be different following a large short-term exposure as compared with the same exposure averaged over a longer period.
3. Variability in sensitivity among different lifestages may not have been fully considered. For example, the prenatal and neonatal periods, childhood, adolescence, and peri-menopausal and senior lifestages, as well as genetic predisposition, are currently not included in standard adult animal bioassays for deriving estimates of cancer potency.

This document provides a background discussion on each of these issues and presents interim guidance and supporting rationales.

[2] A carcinogen acts via a mutagenic mode of action if the carcinogen or its metabolite is DNA-reactive or has the ability to bind to the DNA. Mutagenicity is "the induction of permanent, transmissible changes in the amount, chemical properties or structures of the genetic material. In most cases, mutation involves changes in DNA structure that either have no effect or cause harm" (USEPA, 2005b; Schoeny, 2011).

1.3 Practice of Dose Averaging

Dose averaging refers to the practice of time averaging a short period of exposure or several intermittent short-duration exposure(s) over a longer duration. This practice is also referred to as exposure amortization. It assumes toxicity to be linearly proportional to the magnitude and duration of exposure. For example, it assumes an exposure of 365 µg/kg bw-day for 1 day, 36.5 µg/kg bw-day for 10 days and 1 µg/kg bw-day for 365 days to be toxicologically equivalent, which could be untrue. The risk for the shorter-term exposure could be underestimated. With this practice, daily exposures that exceed the maximum chronic acceptable daily dose (either a TDI or a risk-specific dose) may be incorrectly considered acceptable because they occur for only a short period of time. In the case of threshold carcinogens, this practice raises questions about the magnitude by which the TDI can be exceeded and for what duration before unacceptable chronic health risks (including carcinogenicity) are possible or expected. For non-threshold carcinogens, the practice raises the question of whether a high dose over a short period results in the same lifetime cancer risk as the same total dose over a lifetime. Also at issue is whether the short-term exposure could elicit adverse acute/subchronic non-carcinogenic health effects.

The answers to these questions, in part, depend on the following:

- when (at what lifestage) the excess exposure is expected to occur;
- whether there are any specific sensitivities associated with that lifestage; and
- whether these sensitivities have been accounted for (perhaps through application of uncertainty factors) in the TRV.

2.0 DOSE AVERAGING FOR NON-THRESHOLD CARCINOGENIC EFFECTS

The current practice of characterizing incremental cancer risks associated with less-than-lifetime exposures involves averaging the short period of exposure over a lifetime to calculate the LADD. This practice assumes that the overall incremental cancer risk is a function of the total dose received and is independent of the exposure pattern: a high dose of a carcinogen received over a short period is assumed to be equivalent to the corresponding total dose spread over a lifetime (US EPA, 1986). However, this practice is not based on firm scientific evidence or principles (Hrudey, 1998), and the US EPA (1986) has acknowledged that the approach is fraught with uncertainty; it recommends that risk assessments include a qualitative discussion of the uncertainty of this assumption.

Various groups of scientists have expressed concern that the LADD approach could underestimate cancer risk (Kodell et al., 1987, Chen et al., 1988; Murdoch et al., 1992; US EPA, 2005a; Halmes et al., 2000); the summary of some of these studies is presented in Table 2. In addition, the age at which short-term exposure occurs could influence cancer risk, as different lifestages may vary in susceptibility (Drew et al., 1983; Crump and Howe, 1984; Ginsberg, 2003; US EPA, 2005a, 2005b; Hattis et al., 2004, 2005).

The uncertainty of the practice was identified as an issue "under review" in Health Canada's (2004) guidance on Human Health Preliminary Quantitative Risk Assessment for contaminated sites. Since that publication, Health Canada's CSD has commissioned a series of contractor reports from consulting and academic experts (Brand, 2004; GlobalTox International Consultants, 2005; Wilson Scientific Consulting Inc., 2006; Orr, 2007; Al-Zoughool and Krewski, 2008) to aid in the decision-making on this issue.

Table 2.1 Summary of modelling studies that compare cancer risks from short-term exposure with those from lifetime-equivalent exposure (extent of under/overestimation reported quantitatively for short-term adult exposure only)

Reference	Study type	Qualitative assessment	Range of most likely predicted LADD underestimate to overestimate of risk	Maximum predicted underestimate (overestimate) of risk
Murdoch et al., 1992	Theoretical modelling for 30-day exposures of astronauts aged 25 to 45 to hypothetical carcinogens inside the space station. Both A-D[a] multistage and MVK[b] models were used.	LADD may underestimate or overestimate risks.	–2 to +6 fold (A-D multistage model); –2 to +7 fold (MVK model)	–2 (+33) fold (A-D multistage model); –1.4 (+63) fold (MVK model)
Kodell et al., 1987	The A-D multistage model was used to model intermittent exposure to a hypothetical carcinogen starting at age 0, 10, 20 and 50 for 1, 10 and 20 years. The ratio of excess risk for intermittent dosing relative to predicted excess risk based on LADD was calculated.	LADD underestimates risk maximally when the number of cancer stages is assumed to be 6, the 1st stage is dose-dependent and exposure occurs during years 1–10 of life.	–3 to +14 fold	–3 (> $+10^5$) fold
Chen et al., 1988	The MVK model was used to calculate the ratio of excess risk for short-term exposure to a hypothetical carcinogen to predicted excess risk associated with underlying assumptions of LADD, with various input parameters, including duration of exposure and start time of exposure.	LADD underestimates risk maximally with early-stage carcinogen and exposure early in life.	–2 to +13 fold (initiator); –4.5 to +13 fold (completer); –9 to +9 fold (promoter)	–2 (> +100) fold (initiator); –5 (> +25) fold (completer); –77 (+100) fold (promoter)

[a] Armitage-Doll

[b] Moolgavkar-Venzon-Knudson

2.1 Dose Averaging for Less-Than-Lifetime Adult-Only Exposures

The issue of dose averaging can be confounded by the potential for varied susceptibility among different lifestages. The TRV developed from studies involving adult-only exposure (e.g. occupational studies) may be inadequate to account for earlier sensitive lifestages, especially when short-duration, high-magnitude exposure is experienced during these sensitive time windows. For this reason, less-than-lifetime exposure occurring only during the adult lifestage is addressed first. In this case, the only issue leading to the potential underestimate of health risk is assumed to be the mathematical manipulation of the level of exposure. For example, daily occupational exposures occurring 5 days per week for 48–52 weeks per year are amortized to the equivalent daily dose over 7 days per week for 52 weeks per year (resulting in a lower calculated daily exposure). Amortization of this magnitude is common, as TRVs are often derived from epidemiological studies based in occupational environments. Similarly, animals are dosed 5 days per week in some toxicity studies.

Two general lines of inquiry have been explored to determine the extent to which time averaging may over or underestimate cancer risks in adult-only exposures:

1. Evidence from animal bioassays or epidemiological studies in which the cancer risks estimated from short-term exposures are compared with those derived from adult lifetime exposures.
2. Comparison of the cancer risk estimates from short-term exposures with those derived for lifetime exposures at the LADD-equivalent dose using generally accepted mathematical models of carcinogenesis.

2.1.1 Dose Averaging Implications from Adult Animal Bioassays

Standard carcinogenicity bioassays involve near-lifetime exposures; however, exposures of very limited duration may also result in tumour formation. A literature review by Calabrese and Blain (1999) found 426 chemicals from a broad range of chemical classes that could induce cancer after a single administration in a large number of animal models. Most of these chemicals, if not all, were found to be genotoxic. Thirty nine percent caused more tumours, 22% caused fewer tumours, and the remaining 39% showed similar tumourigenic responses when the carcinogen was administered as a single dose as compared with the same dose fractionated over a lifetime. However, Calabrese and Blain (1999) and others (Ginsberg, 2003) did not consider varied lifestage susceptibility when analyzing the available data, which involved a single exposure at different lifestages (i.e. fetal, neonatal).

Stop-exposure studies (summarized in Table 2.2) illustrate the influence of exposure schedule and duration on cancer risk. Exposures were stopped after only a portion of the animal's lifespan, and the animals were observed long enough to measure tumour development.

Table 2.2 Summary of studies comparing cancer risks from short-term (adult-only) exposure with those from lifetime-equivalent exposure (with same total dose)[a]

Reference	Study type	Qualitative assessment	Range of most likely predicted LADD underestimate to overestimate of risk	Maximum predicted underestimate (overestimate) of risk
	Animal experiments			
Halmes et al., 2000	Animal stop-exposure—data from 11 National Toxicology Program studies (adult animals—male rats or mice). Cancer potency was estimated using 2-year continuous bioassay data with or without inclusion of stop-exposure data.	Tumour responses in the stop-exposure experiment were underpredicted by continuous exposure data at 34/59 tumour sites for 6/11 chemicals, and overpredicted at 2/59 tumour sites for 2/11 chemicals. Prediction was accurate for 26/59 tumour sites for 9/11 chemicals.	Undefined	Undefined
		Inclusion of stop-exposure data in ED_{01}[b] estimation (as compared with using continuous bioassay data alone) led to a decrease for 63% of the chemical/tumour/site combinations and an increase for 17% of the chemical/site combinations, mostly within one order of magnitude. 15% (of all tumour sites examined) showed a greater than 10-fold decrease (greater risk or potency) in ED_{01}, implying a higher risk with shorter exposure.	Undefined	Undefined
		The "equivalent averaging times"[c] for the stop-exposures were generally longer than the actual exposure durations but less than 104 weeks for 12 of the 14 dose groups for which this comparison was made. The median "equivalent averaging time" for all the groups was 62 weeks, indicating that averaging stop-exposure duration over a lifetime (LADD) would underestimate the risk by a median factor of 2.	–5 to +2 fold	–5 (+2) fold

Table 2.2 – cont'd ➜

Reference	Study type	Qualitative assessment	Range of most likely predicted LADD underestimate to overestimate of risk	Maximum predicted underestimate (overestimate) of risk
Drew et al., 1983	Animals exposed to constant concentrations of vinyl chloride (adult animals—rats, 2 strains of mice, hamsters) by inhalation. Animal age at the start of exposure and exposure duration were varied among different exposure groups.	For most of the animal species studied, exposure from months 2–8 of life produced higher tumour frequency than exposure at later lifestages for the same duration (8–14, 14–20 or 20–26 months of age), possibly because animals died before a potential tumour could be expressed in the latter groups.	Undefined	Undefined
Hattis et al., 2004	Animals—rats and mice exposed to four types of ionizing radiation at different stages of life	On the basis of a total of 138 group tumour incidence observations, dosage delivered to older animals (6–12 or 19–21 months old) appeared to be 3 fold less effective than a similar dosage delivered to young adult animals (3–3.5 months), suggesting greater sensitivity during early adulthood.	Undefined	Undefined
	Epidemiological studies			
Hauptmann et al., 2000	Case-control study of lung cancer and smoking in adults (4300 cases). The effect of smoking pattern on lung cancer risk was examined using a linear model taking into consideration that different exposure periods vary in their contribution to the overall cancer risk.	The number of cigarettes smoked within 5–15 years prior to patient interview strongly determined lung cancer risk; the number smoked more than 20 years earlier contributed minimally to risk. The pattern corresponds to an observed decrease in risk corresponding to the time since smoking cessation. Authors concluded that use of cumulative or average dose may not be appropriate for estimating lung cancer risk.	Undefined	Undefined
Hauptmann et al., 2002	Pooled data from two German case-control studies (2652 cases) on asbestos and lung cancer were assessed in terms of various exposure metrics.	The results suggested that cancer risk increased for 5–15 years after exposure and then declined. Other studies have indicated a 20–40 year latency period for asbestos-induced lung cancer. Dose averaging over a lifetime would underestimate the risk for people whose remaining lifespan is greater than the latency period and would overestimate the risk for people whose remaining lifespan is shorter than the latency period.	Undefined	Undefined

Table 2.2 – cont'd ➜

Reference	Study type	Qualitative assessment	Range of most likely predicted LADD underestimate to overestimate of risk	Maximum predicted underestimate (overestimate) of risk
Elwood et al., 1985; Elwood, 1992	Histories of exposure to sun of 595 patients with malignant melanoma in Western Canada were examined in a case-control study.	Significant increase in risk was correlated with summer vacation and recreational activities with intense sun exposure. A moderate amount of total occupational exposure (likely from intermittent seasonal exposure) increased the risk; further increased exposure (> 200 whole body equivalent hours of exposure per season associated with long continuous exposure) had no effect or resulted in decreased risk (for men). At the same total sun exposure, the relative risk of melanoma from short-term intermittent recreational exposure exceeded long-term occupational exposure by up to 2 fold.	+1 to –2 fold	–2(+1)

[a] Adapted from Tables 4.5-1 and 4.5-2 in Orr (2007); edited to exclude studies in which juvenile exposures were compared with adult exposures.

[b] ED_{01} is the maximum likelihood estimate of the dose corresponding to a 1% additional cancer risk.

[c] Equivalent averaging time is the length of time over which stop-exposure doses have to be averaged so that the observed response falls exactly on the fitted dose-response curve developed from the continuous exposure (i.e. 104 weeks) data.

Halmes et al. (2000) evaluated cancer data from 12 similar United States National Toxicology Program animal bioassays in which both chronic lifetime and stop-exposure dosing protocols (using male rats except for 1,3-butadiene, to which male mice were exposed) were followed. The Weibull Model was fitted first to the chronic data only and then to the combined chronic and stop-exposure data adjusted to average lifetime exposure. Tumours developed following exposure to 11 chemicals (acting through different modes of action), some at multiple sites, totalling 59 chemical/site combinations. The same response rate was observed for 44% of the chemical/tumour site combinations. However, for 46% of the chemical/tumour site combinations, the response rate was higher in the stop-exposure groups than the chronic lifetime exposure groups. About 5% showed a lower response in the stop-exposure groups than the chronic lifetime exposure groups. Therefore, the assumption of equivalent cancer risk at equivalent total doses (i.e. that the product of concentration and time is constant independent of the exposure pattern) was incorrect at least half of the time. Combining stop-exposure and continuous exposure data in ED_{01}[3] estimation showed varied effect. Inclusion of responses from the stop-exposure groups led to a decrease in the ED_{01} (greater risk or potency) for 63% of the chemical/tumour/site combinations and an increase in the ED_{01} (lesser risk or potency) for 17% of the chemical/site combinations, mostly within one order of magnitude. While the overall change was less than 2-fold (in either direction) for 36% of the tumour sites examined, approximately 15% (of all tumour sites examined) showed a greater than 10-fold decrease (greater risk or potency) in ED_{01}, implying a higher risk with shorter exposure. The largest reduction was 102-fold for lymphomas following 1,3-butadiene exposure.

Halmes et al. (2000) also evaluated dose averaging by determining the "equivalent averaging time". Equivalent averaging time is the length of time over which stop-exposure doses have to be averaged so that the observed response falls exactly on the fitted dose-response curve developed from the continuous exposure (i.e. 104 weeks) data. This method of evaluation has a direct implication for cancer risk assessment. The stop-exposure studies exposed animals for varying durations that ranged from 13 weeks to 66 weeks. For most endpoints, the "equivalent averaging times" were generally longer than the actual exposure durations but less than 104 weeks for 12 of the 14 dose groups for which this comparison was made. The median "equivalent averaging time" for all the groups was 62 weeks, indicating that averaging the stop-exposure dose over a lifetime (i.e. LADD) would underestimate cancer risk by a median factor of 2 (ranging from an overestimation of 2-fold to an underestimation of 5-fold).

In addition to duration-related variability (i.e. short-term versus long-term exposures), carcinogenic sensitivity may not be constant throughout the adult period. On the basis of their analysis of animal (rats and mice) experimental data involving four different types of ionizing radiation, Hattis et al. (2004) demonstrated that the dosage delivered to older animals (6–12 months or 19–21 months old) appeared to be several-fold less effective than a similar dosage delivered to young adults (3–3.5 months old), suggesting greater sensitivity for exposures in early adulthood.

In summary, experimental data with animals suggest that averaging short-term exposure over a lifetime results in uncertainties and may overestimate or underestimate the risk when exposure occurs during adulthood. The level of underestimation or overestimation is generally within an order of magnitude for the substances studied. However, many carcinogens found at contaminated sites have not been studied in this manner.

2.1.2 Dose Averaging Implications from Adult Exposures in Epidemiological Studies

The available epidemiological data on the effect of exposure patterns on cancer risks (summarized in Table 2.2) are limited, lung and skin cancer being the most frequently studied.

A review (Wilson Scientific Consulting Inc., 2006) of the literature on cancer risk from smoking indicates a general scientific consensus that cancer risk decreases for individuals who quit smoking when compared with those who continue to smoke, the extent of the reduction lessening as the age of quitting increases. The review concluded that an appreciable amount of cancer risk is removed 10 years after smoking cessation. However, although smoking reduction may also lead to reduced lung cancer risk, the conclusion did not consider the intensity of smoking or the age of the smoker. Smoking is a unique activity that involves inhaling a high dose of a mixture of carcinogenic and non-carcinogenic chemicals, which include irritants and pharmacologically active levels of nicotine. The effects of both psychological and physical addiction as well as other socioeconomic factors may not have been accounted for in the analyses. Therefore, the exposure–risk relationship observed for smoking may not be applicable to carcinogens and exposures typical of contaminated sites. In addition, the available analysis of the smoking data lacks a quantitative comparison of the cancer risks predicted by LADD and alternative approaches with the observed cancer risks as a function of smoking intensity (dose) and duration.

Hauptmann et al. (2002) investigated lung cancer risk associated with occupational exposure to asbestos in two German case-control studies. The data suggest that an individual's lung cancer risk increased for 5–15 years after exposure and then declined. The risk declined to about one-half after more than 20 years from the final exposure. When individual risks were modelled and compared, the risk was higher and peaked earlier at high exposure rates as

[3] Maximum likelihood estimate of the dose corresponding to a 1% additional cancer risk.

compared with lower exposure rates (5 fiber-yrs/yr for 5 years versus 0.5 fiber-yrs/yr over 50 years). The result suggests that dose averaging over a lifetime would underestimate the risk, especially for people whose remaining lifespan is longer than the latency period. On the other hand, the risk would be overestimated for people whose remaining lifespan is shorter than the latency period.

Case control studies of the incidence of melanoma or basal cell carcinoma involving patients 20–79 years of age with a recent diagnosis in Western Canada (Elwood et al., 1985) found an individual's total dose alone did not determine cancer risk, as the intensity of exposure also played a role. Activities that likely involved more intense sun exposure (vacation and recreation) conferred a greater level of risk (by up to 2-fold) than if the same dose had been achieved by predominantly occupational exposure. A moderate amount of occupational sun exposure (likely from intermittent seasonal exposure) increased the risk, but further increase in exposure (typical of chronic occupational exposure) either had no effect or resulted in decreased risk (for men) (Elwood, 1992). Other major studies showed a similar pattern following intermittent exposures, although results from the northern hemisphere studies are more definitive than from Australian studies (Kricker et al., 1995), partly because the total dose received in Australia is so much greater (Elwood, 1992).

The limited human data associated with short-term or intermittent exposure support the notion that averaging short-duration or intermittent exposure over a longer time period may not be appropriate for predicting cancer risk.

2.1.3 Theoretical Cancer Modelling Studies of Less-Than-Lifetime Exposure

Mathematical models of cancer, such as the A-D multistage model and MVK model (the latter model is also known as the two stage birth-death-mutation model), are generally compatible with the current understanding of the mechanism of carcinogenesis. The A-D multistage model assumes cancer to be the end result of a normal cell going through a finite number (e.g. k) of irreversible independent transitions (stages) that must take place in a specific order (Armitage, 1985; Al-Zoughool and Krewski, 2008). The MVK model assumes that the clonal expansion of cancer involves two discrete phases: initiation (due to genetic damage) and malignant conversion with progression (Al-Zoughool and Krewski, 2008). Although these models have not been validated (United Kingdom Department of Health, 2004), they have been used to describe the age-dependent rate of cancer formation and to explore the extent to which the LADD approach could over or underestimate cancer risk resulting from less-than-lifetime exposure scenarios (Kodell et al., 1987; Murdoch and Krewski, 1988; Chen et al., 1988; Murdoch et al., 1992, Al-Zoughool and Krewski, 2008). These analyses may provide insight into the upper bound estimate of the level of over or underestimation of the risk.

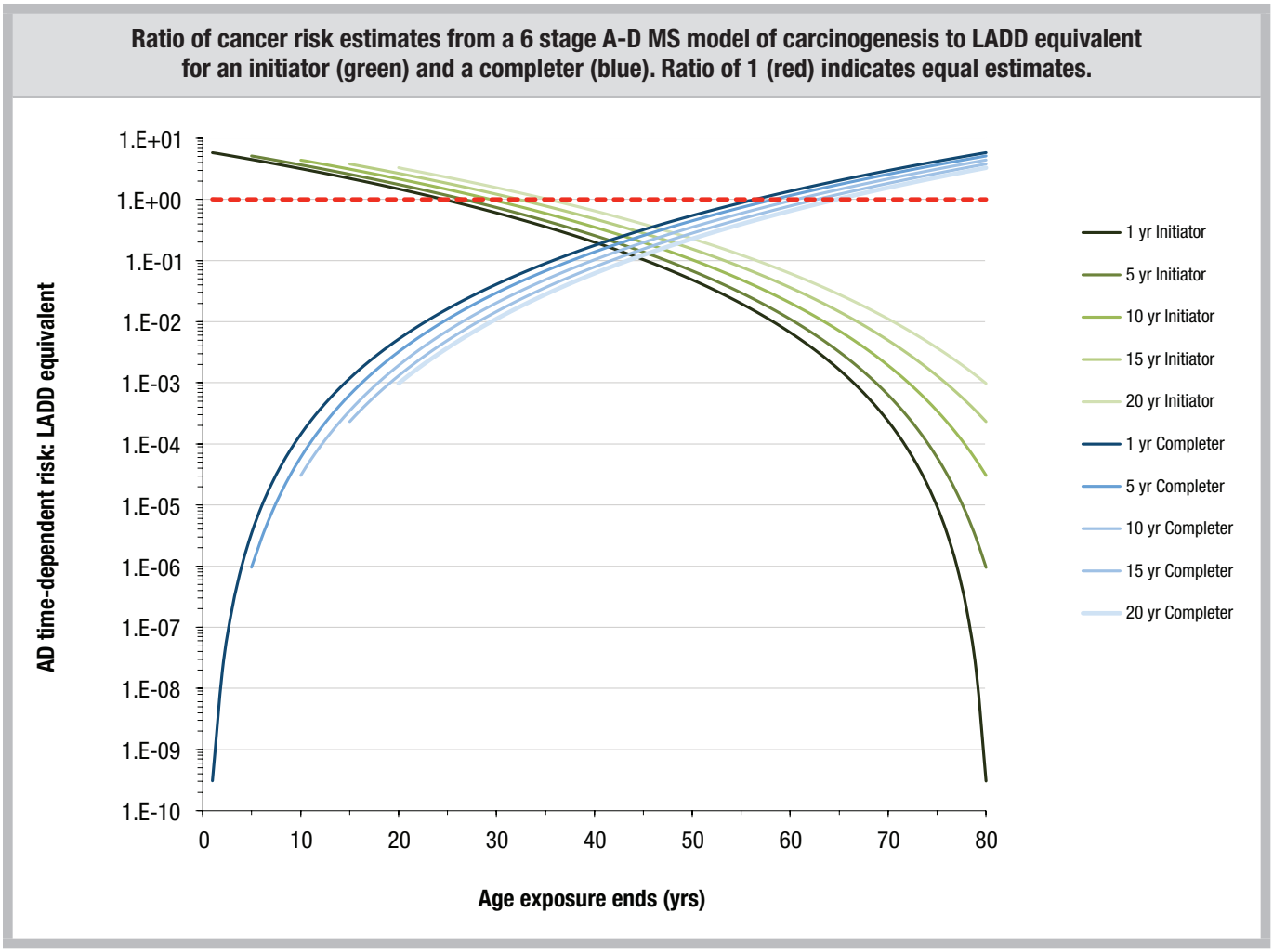
Using the A-D multistage time-to-tumour model, a number of publications (Murdoch et al., 1992; Al-Zoughool and Krewski, 2008; Kodell et al., 1987) have demonstrated the propensity of LADD to over or underestimate cancer risk under certain exposure scenarios. The theoretical upper bound of underestimation by the LADD approach was also estimated. The consensus is that the LADD approach can over or underestimate cancer risks for less-than-lifetime exposures depending on the exposure. The greatest extent of underestimation was postulated for two general scenarios: short-term exposures in early life to initiators (carcinogens that increase the rate of the first stage of carcinogenesis) and short-term exposures late in life to completers (carcinogens that increase the rate of the last stage of carcinogenesis, Chen et al., 1988). In both cases, LADD can underestimate cancer risk by up to a factor of 6. When short-duration exposure occurs in an adult's mid-life period, the extent of underestimation is less than 2- to 3-fold. Depending on the mode of action, cancer risk from short-term exposure may also be overestimated by up to several orders of magnitude.

The relationships between the prevalence and magnitude of potential under and overestimates of cancer risk using the LADD approach are illustrated in Figure 2.1. This figure compares the relative risk estimates generated using a 6-stage A-D multistage model (to estimate cancer risks for time-dependent exposure patterns) with those calculated using an "equivalent" LADD (a time-weighted average dose assuming constant lifetime exposure). The value of 1 on the Y axis represents equivalent risk estimates. Values greater than 1 represent cases in which LADD underestimates cancer risks relative to the time-dependent risk model, and values smaller than 1 represent cases in which LADD overestimates those risks. The figure illustrates that, except for the specific cases discussed above, the LADD is more likely to overestimate cancer risk, and the magnitude of potential overestimation is much greater than the magnitude of underestimation.

It is important to note that the difference in cancer risk estimates between the models is dependent on the number of stages considered in the A-D multistage model, which stage is affected and the age at first exposure. Figure 2.1 illustrates a comparison using the 6-stage A-D multistage model and an assumption that only one stage (i.e. first or last stage) is dose-related. The difference between the models in cancer risk estimates will be smaller if one uses a lower number of cancer stages in the A-D multistage model. The modelled cancer risk estimates become approximately equivalent with a 2-stage A-D model (assuming carcinogenesis has only two stages).

The results from the MVK model generally parallel those from the A-D multistage model exercises (Chen et al., 1988; Murdoch et al., 1992). The model predicts LADD may over or underestimate cancer risks depending on the cell growth rate, time of first exposure, duration of exposure and the type of carcinogen. The maximum underestimate of risk reported by Chen et al. (1988) using the LADD approach would occur with early-life, shorter exposures to an initiator (maximum 7-fold underestimate) or with longer duration, late-life exposures to a completer (maximum 4.5-fold underestimate). When exposure takes place during mid-life, the degree to which LADD can underpredict cancer risk (up to 2-fold) for initiators using the MVK model is generally quite comparable with the A-D multistage model prediction (Chen et al., 1988; Murdoch et al., 1992).

Figure 2.1 Relative cancer risk estimates for various ages and durations of adult exposure calculated using a 6-stage Armitage-Doll multistage (MS) model for estimating cancer risks for time-dependent exposure patterns versus lifetime average daily dose (LADD). Only one stage was assumed to be dose-related in the modelling, the first stage for "initiators" and the last (or kth) stage for "completers". A value of 1 on the Y axis (indicated by the red horizontal dotted line) represents equivalent risk estimates. Values greater than 1 represent cases in which LADD underestimates cancer risks, and values smaller than 1 represent cases in which LADD overestimates risks.



2.1.4 Summary for Dose Averaging for Less-Than-Lifetime Adult Exposure

Evidence from animal experiments, epidemiological studies and theoretical modelling studies supports the conclusion that exposure pattern has an effect on lifetime cancer risk. Averaging less-than-lifetime exposure over a lifetime using LADD may underestimate or overestimate cancer risks, depending on the timing of exposure and the mode of action of the carcinogen. The degree of underestimation seems generally to be confined to within an order of magnitude and is approximately 2-fold for short exposure during all but the very late stages of adulthood. Theoretical modelling predicts up to a 6-fold underestimation of risk for exposure to a completer only late in life; however, most chemicals act through multiple mechanisms, and few exclusive completers have been identified. The original multistage A-D model assumes that cancer incidence increases with age at a constant rate. The review by Al-Zoughool and Krewski (2008) indicates that this assumption does not apply to the incidence of prostate and breast cancers, which increase until age 40 and 50 and decline thereafter; the incidence of most cancer types declines after the age of 80. The multistage model may therefore overestimate cancer rates in the elderly, and LADD may not underpredict cancer risk from less-than-lifetime exposure to (theoretical) completers late in life as much as the model suggests.

Overall, the limited evidence currently available suggests dose averaging over a lifetime (LADD) overestimates as frequently as it underestimates cancer risk for short-term exposure. However, for adult exposures to mutagenic carcinogens (e.g. initiators), the underestimation of cancer risk is insignificant in most cases. Adjustment to correct for underestimation of cancer risk resulting from using the LADD approach for less-than-lifetime exposures in adults is therefore not recommended (i.e. the status quo is maintained).

2.2 Dose Averaging for Less-Than-Lifetime Early-Life Exposure

Cancer slope factors are generally derived from adult human epidemiological studies or standard chronic adult rodent bioassays. The US EPA (2005a) conducted a comprehensive review of cancer risk associated with early-life exposure to determine whether specific age-dependent adjustments of adult cancer slope factors were needed when assessing cancer risk from early-life exposure.

The review found limited cancer epidemiological data involving childhood exposure to radiation and chemotherapeutic agents. A review of available animal studies (Barton et al., 2005; Chhabra et al., 1993; Peto et al., 1984; Vesselinovitch et al., 1979) indicated that early-life exposures (i.e. perinatal) usually resulted in a higher tumour incidence later in life than standard adult-only exposures.

These findings are consistent with the current understanding of biological processes involved in carcinogenesis and are supported by other reviews (McConnell, 1992; Miller et al., 2002; US EPA, 1996), which found the following:

- Tumours usually occur at the same sites following either perinatal or adult exposure.
- Perinatal exposure followed by adult exposure usually increases the percentage of treated animals bearing tumour or reduces the latency period before tumours are observed as compared with adult-only exposures.

The US EPA (2005a) identified several factors that may contribute to increased susceptibility to carcinogens in early life:

- Differences in the capacity to metabolize and clear chemicals at different ages can result in larger or smaller internal doses of the active agent(s), either increasing or decreasing risk (Ginsberg et al., 2002; Renwick, 1998).
- More frequent cell division during development can result in enhanced fixation of mutations because of the reduced time available for repair of DNA lesions, and clonal expansion of mutant cells results in a larger population of mutants (Slikker et al., 2004).
- Some embryonic cells, such as brain cells, lack key DNA repair enzymes.
- Some components of the immune system are not fully functional during development (Holladay and Smialowicz, 2000; Holsapple et al., 2003).
- Hormonal systems operate at different levels during different lifestages (Anderson et al., 2000).
- Induction of developmental abnormalities can result in a predisposition to carcinogenic effects later in life (Anderson et al., 2000; Birnbaum and Fenton, 2003; Fenton and Davis, 2002).
- While tumour promotion processes can be very dependent upon the duration of promotion, initiation processes can occur in relatively brief periods.
- Most tumours take extended periods to develop, which means that damage occurring earlier in life is more likely to result in tumours before death than would exposures that occur later in life.

The US EPA (2005a) compared the cancer potencies from early-life exposure with the cancer potencies from adult exposure in repeated (continuous) dosing studies taken from the published literature. Studies included in the analysis involved a) exposure of animals either only during the juvenile or adult period and followed through adulthood to assess tumour incidence; or b) exposure of animals beginning either in the juvenile or adult period, but once begun continuing through life. Cancer potencies were estimated by fitting the one-hit model, or a restricted form of the Weibull model, to the data for each age group. The analysis for the six carcinogens

(benzidine, diethylnitrosamine, 3-methylcholanthrene, safrole, urethane and vinyl chloride) with a mutagenic mode of action is most informative. The results indicate that the early lifestages can be, but are not always, much more susceptible to cancer development than when exposure occurs in the adult lifestage. The ratio of tumour incidence from early life to adult exposure varies by chemical, sex and species with the weighted geometric mean ratio estimated at 10.4.

The US EPA (2005a) performed a similar analysis of acute dosing studies (which generally compared a single exposure during the juvenile period with identical or similar exposure in adult animals). The results[4] supported the concept that early-lifestage exposure to carcinogenic chemicals with a mutagenic mode of action leads to increased tumour incidence when compared with adult exposure of a similar dose and duration.

On the basis of the analysis involving repeated (continuous) dosing studies, the US EPA (2005a) recommended adjusting the adult cancer slope factor by a factor of 10 for exposures to mutagenic carcinogens occurring during the first 2 years of life. Pharmacokinetic and pharmacodynamic differences between children and adults are greatest during the first 2 years of life (World Health Organization, 2006), which corresponds to the period of birth to weaning in laboratory rodents (Hattis, 2005; WHO, 2006).

The US EPA (2005a) considered the available data insufficient to calculate a specific adjustment factor for the period from 2 through 15 years of age, which represents middle adolescence and follows the period of rapid developmental changes during puberty. The US EPA therefore selected a 3-fold adjustment as it is the geometric mean between the 10-fold adjustment for the first 2 years of life and a unity adjustment for adult exposure. The US EPA recommends that these default age-dependent adjustment factors be applied only when chemical-specific data on early-life exposure are absent.

Although the limited data for carcinogens with a non-mutagenic mode of action (e.g. hormonally mediated) suggest increased susceptibility when exposure occurs perinatally, the US EPA (2005a) considered the data inadequate to derive a generic adjustment of cancer response. More research is needed, particularly because it was observed that tumours arising from hormonally active chemicals appeared to involve different sites when exposure occurred during early life versus adulthood.

The California Environmental Protection Agency (CalEPA, 2009) released its findings on a similar study it undertook to address age-related cancer. This study compared cancer potencies (estimated by applying the linearized multistage [LMS] model to the dose-response data from animal experiments) from early-life exposures (exposed during the prenatal, postnatal or juvenile period) with exposure at an older age, preferably during adulthood. CalEPA used the full distribution of the cancer slope to derive the ratios of cancer potencies from early-life to adult exposures with adjustment for time to manifest tumour (i.e. to account for the longer available time the young animals had from exposure to tumour development). Each chemical was represented by a single distribution based on cancer potencies estimated from one or more studies and from all tumour sites.

The medians of the postnatal age sensitivity factor (ASF), estimated from data on 18 carcinogens (55 distributions), and the juvenile ASF, estimated from data on 5 carcinogens (7 distributions), were reported as 13.5 and 4.5 respectively. Because of the limited database and the broad distributions of results for different chemicals, CalEPA found no basis for specifying a default ASF with greater than half-log precision (i.e. values of 1, 3, 10, 30, etc). Further, rodents are born at a stage of maturity that approximates that of a third-trimester human foetus. Therefore, in the absence of chemical-specific data, CalEPA recommended applying a default ASF of 10 for the third trimester to age 2 years (totalling 2.25 years) and a factor of 3 for ages 2 through 15 years to account for potential higher sensitivity during early lifestages. While the same values were selected by US EPA (2005a) to be applied only to carcinogens with a mutagenic mode of action, CalEPA will apply these factors to all carcinogens. CalEPA (2009) included in its analysis three non-genotoxic carcinogens and found evidence that early life is a susceptible time for a carcinogen thought to act through a non-mutagenic mode of action, e.g. diethylstilbestrol (DES). CalEPA's rationale for not restricting ASF to chemicals acting via a mutagenic mode of action includes the potential problems of defining "mutagenic mode of action" when applied narrowly and the possibility of carcinogens with multiple modes of action that dominate at different lifestages (CalEPA, 2009).

2.3 Dose Averaging for Prenatal Exposure (Transplacental Carcinogenesis)

A number of agents are suspected to be transplacental carcinogens, i.e. in utero exposure to these agents leads to cancer development later in life, involving either a mutagenic or a non-mutagenic mode of action. Most data are from animal studies, such as those involving DES, genistein, tamoxifen, polycyclic aromatic hydrocarbons (PAHs), polybrominated biphenyls, polychlorinated dibenzo-p-dioxins (dioxin; reviewed in Birnbaum and Fenton, 2003), arsenic (Waalkes et al., 2004) and nitrosamines (Mohr et al., 1983). In humans, only radiation and DES have been shown to cause cancer following in utero exposures (Anderson et al., 2000; Barton et al., 2005; and Birnbaum and Fenton, 2003). Other chemicals suspected to be transplacental carcinogens

[4] Based on acute dosing carcinogenic data for eight chemicals with a mutagenic mode of action: benzo[a]pyrene, dibenzanthracene, diethylnitrosamine, dimethylbenzanthracene, dimethylnitrosamine, ethylnitrosourea, methylnitrosourea, urethane.

on the basis of human data include aflatoxin B1 and the hormones used for assisted reproduction (in vitro fertilization). These substances are not typically found at federal contaminated sites; moreover, for many substances that are found at contaminated sites, the data on transplacental carcinogenesis are available only from animal studies.

Some chemicals may be acting as initiators following in utero exposures or prezygotic exposure of the male parent, with cancer formed only upon subsequent postnatal promotion and/or additional exposures (i.e. in utero exposure creates altered susceptibility to cancer later in life). This effect has been seen experimentally with various chemicals, including dioxin/dimethylbenzantracene (DMBA; Brown et al., 1998), 3-methylcholanthrene/butylated hydroxytoluene (Gressani et al., 1999), genistein or atrazine/DMBA (Hilakivi-Clarke et al., 1999; Fenton and Davis, 2002) and N-methyl-N-nitrosourea or PAHs/phenobarbital (Diwan et al., 1989). In utero initiation/postnatal promotion has been demonstrated in humans only for DES and radiation (Yamasaki et al., 1992).

The prenatal to adult cancer potency ratio has not been considered in the US EPA (2005a) supplemental guidance. The CalEPA (2009) has conducted a probabilistic analysis of the prenatal to adult potency ratio. The prenatal age window showed an increased sensitivity to the majority of the 14 carcinogens (22 potency ratio distributions) analyzed. The median of the prenatal ASF distribution was 2.9. However, because of the limited database and the considerable variability in available data, no recommendation on a default adjustment factor was proposed for prenatal exposures in the first and second trimesters. As rodents are born at a stage of maturation similar to that of a third-trimester human foetus, the trimester is included in the default ASF of 10 proposed for up to 2 years of age (i.e. total duration of 2.25 years). No other major regulatory agency has a default position for adjustment of risk calculations for prenatal exposures. While CalEPA (2009) illustrated how an ASF of 10 can be applied when the daily exposure (mg/kg-d) is known, the agency has not provided sample risk calculations for human exposure from known environmental concentrations.

Physiologically based pharmacokinetic (PBPK) modeling of transplacental transfer could theoretically better define the magnitude of increased susceptibility in the foetus. However, validated PBPK models are unlikely to become available in the near future, as the necessary data for modelling and reliable markers of foetal exposure are lacking, and the models themselves require further refinement (Anderson et al., 2000). Efforts to advance knowledge on issues such as the temporal profile and gene polymorphism in enzymes involved in carcinogen activation/detoxification and DNA repair enzymes in the foetus would facilitate development of better PBPK models. More work with animal models is needed to identify transplacental carcinogens and their mechanism of action, including interaction with target genes.

2.4 Dose Averaging for Less-Than-Lifetime Exposure during Puberty

Mutagenic carcinogens are generally more effective in rapidly dividing tissues. The higher rates of cell division provide more opportunities for carcinogens to interact with DNA and less time for DNA repair prior to cell division, which results in increased probability of initiation activity. During puberty, there is dramatic growth in reproductive and other related organs, including some parts of the brain, potentially making them more susceptible to mutagenic carcinogens acting at those sites.

Changes in physiological and biological processes during puberty could also alter susceptibility to the effects of some non-mutagenic carcinogens (e.g. endocrine-disrupting chemicals). On the basis of its analysis of the limited available data, the US EPA Science Advisory Board (US EPA, 2004) concluded that altered sensitivity to the development of cancer may occur when exposure takes place during puberty as compared with other exposure time windows.

3.0 PROPOSED INTERIM MEASURE FOR HUMAN HEALTH RISK ASSESSMENT FOR LESS-THAN-LIFETIME EXPOSURE TO CANCER-CAUSING AGENTS AT CONTAMINATED SITES

The CSD provides this interim guidance with regard to HHRA of carcinogenic agents, including short-term exposure and dose averaging. Risk assessments submitted to CSD should provide a rationale taking into consideration the mode of action at the tumour site in question.

3.1 Assessment of Cancer Risk for Non-Threshold Carcinogenic Effects

3.1.1 Carcinogenic Effects Acting Through a Mutagenic Mode of Action

The US EPA (2005 a, b) provides one of the most comprehensive analyses of the available data related to increased sensitivity when exposure to a carcinogen with a mutagenic mode of action occurs at early lifestages. As an interim measure, CSD has adapted the US EPA approach for contaminated site risk assessments.

The US EPA's default adjustment factor of 10 is supported by LMS modelling studies (Al-Zoughool and Krewski, 2008) indicating that a default factor of 6 should be applied to LADD-based cancer risk estimates for mutagens (i.e. to account for potential increased effectiveness of early-life exposure to an initiator). An additional factor of 1.6 may be applied to slope factors derived from rodent bioassays in which exposure begins in early adulthood (6–8 weeks of age), to give a total adjustment of 10 (6×1.6). This additional factor (1.6) is needed to account for the neonatal/infant period (i.e. from birth to 6–8 weeks of age).

This cancer risk assessment approach takes into account the varying sensitivity of different lifestages to cancer effects. The ILCR is estimated by summing the risk from each discrete exposure period. For non-threshold carcinogens acting through a mutagenic mode of action, it is recommended that ADAFs be applied to the cancer slope factor (or inhalation unit risk) with exposure averaged over a lifetime, to account for the sensitivity of the age-dependent exposure period. This approach can be illustrated by the equations below.

ILCR from oral exposure can be estimated using the following equation:

$$ILCR = \sum_i (LADD_i * SF_i)$$

$$= \sum_i (LADD_i * SF * ADAF_i)$$

Where:
$LADD_i$ = dose received during lifestage i averaged over a lifetime
SF_i = age-specific slope factor
SF = adult cancer slope factor (per mg/kg-d)
$ADAF_i$ = age-dependent adjustment factors for lifestage i

For exposure by inhalation, the following equation applies:

$$ILCR = \sum_i (C_{ai} * TR_i * UR * ADAF_i)$$

Where:
C_{ai} = concentration in air during lifestage i (mg/m^3)
TR_i = fraction of time exposed (yr/80 yr)
UR = adult cancer unit risk (per mg/m^3)
$ADAF_i$ = age-dependent adjustment factors for lifestage i

LADD is defined by the following equation:

LADD (mg/kg-d) = [ER * ED]/Lifetime or

LADD (mg/kg-d) = [C * IR * AF * ED] / [BW* Lifetime]

Where: ER = exposure rate (mg/kg-d)
C = chemical concentration in the media (mg/m^3 or mg/kg)
IR = intake rate of medium (m^3/day or kg/day)
AF = medium-specific absorption factor
ED = exposure duration (days)
BW = body weight (kg)
Lifetime = days in a lifetime = 365 d/yr * 80 yr

$LADD_i$ is defined as the dose received during lifestage i averaged over a lifetime and can be represented by the following equation:

$LADD_i$ (mg/kg-d) = [C_i * IR_i * AF * ED_i] / [BW_i * Lifetime]

Where: C_i = chemical concentration in the media a person is exposed to during lifestagei (mg/m^3/ or mg/kg)
IR_i = intake rate of medium during lifestage$_i$ (m^3/day or kg/day)
AF = medium-specific absorption factor
ED_i = exposure duration during lifestage$_i$ (days)
BW_i = body weight during lifestage$_i$ (kg)
Lifetime = days in a lifetime = 365 d/yr * 80 yr

The US EPA's ADAFs have been adjusted to fit the age groups presented in the PQRA (Health Canada, 2004). Table 3.1 summarizes the default adjusted ADAFs that CSD recommends for contaminated site risk assessments of non-threshold carcinogens with a mutagenic mode of action. These default factors can be applied when age-specific cancer slope factors, age-specific inhalation unit risks or chemical-specific data are not available. In scenarios where exposure periods do not match the CSD's age groups, CSD recommends that the US EPA's ADAFs be applied. For example, if exposure occurs only between 7 months and less than 2 years of age, the adjustment factor of 10 would apply. Likewise, if exposure occurs only between 12 and < 16 years of age, the ADAF of 3 would apply. Worked examples are illustrated in Section 4.

When age-specific cancer slope factors, age-specific inhalation unit risks or chemical-specific data are available for a susceptible lifestage, it is preferable to use these data directly to evaluate risks for the chemical and the lifestage on a case-by-case basis. In these cases, such as vinyl chloride, application of default ADAFs would not be appropriate. The US EPA recommends twice the adult inhalation unit risk to be applied for estimating incremental cancer risk from continuous exposure to vinyl chloride from birth.

For intermittent exposures, the total cancer risk will be the sum of each discrete exposure with lifestage-specific potency and exposure averaged over a lifetime.

Table 3.1 Recommended interim adjusted age-dependent adjustment factors (ADAFs) for cancer risk assessment at contaminated sites for carcinogenic effects via a mutagenic mode of action

Lifestage	Age	Adjusted age-dependent adjustment factor (ADAF)[a]
Infant	0–6 months	10
Toddler	7 months–4 years	5[b]
Child	5–11 years	3
Teenager	12–19 years	2[c]
Adult	20+	1

[a] US EPA (2005 a, b), except as noted.

[b] $ADAF_{7\ mo-4\ yr}$ = ($ADAF_{0-<2}$ * D7 mo-1 / $D_{7\ mo-4}$) + ($ADAF_{2-4}$ * D_{2-4} / $D_{7\ mo-4}$) = 10 * 1.5/4.5 + 3 * 3/4.5 = 5, and D_i = exposure duration in years

[c] $ADAF_{12-19}$ = ($ADAF_{12-<16}$ * D_{12-15} / D_{12-19}) + ($ADAF_{16+}$ * D_{16-19} / D_{12-19}) = 3 * 4/8 + 1 * 4/8 = 2, and D_i = exposure duration in years

The prenatal period (in utero) may be a sensitive window of exposure for some cancers, and an ADAF of 3 (or 2) may not be sufficient to address increased sensitivity during puberty, but further study is needed to delineate more accurately the magnitude of increased sensitivity. CSD will continue to evaluate the issue as new research data become available and as other regulatory agencies consider this issue. In the interim, CSD recommends addressing the risks associated with mutagenic carcinogen exposure during these lifestages on a case-by-case basis.

To date, among the carcinogens for which CSD provides TRV values, the US EPA (2009, 2011a) has identified carcinogenic PAHs, trichloroethylene and vinyl chloride as acting through a mutagenic mode of action. After a toxicological review, the US EPA (2010) proposed that chromium (VI) is "likely carcinogenic to humans" via the oral route of exposure and hypothesized a mutagenic mode of action for its carcinogenicity. This US EPA report is currently undergoing review (US EPA, 2011b).

3.1.2 Carcinogenic Effects Acting Through an Unknown Mode of Action

For carcinogenic effects with an unknown mode of action or for which the burden of proof for a threshold mode of action has not been met, CSD recommends treating the effect as non-threshold. The mathematical equations used to estimate cancer risk for mutagenic carcinogens can be applied in these situations. If chemical-specific data are available on quantitative differences between early lifestages and adults, an analysis of the differences could be used to adjust risk estimates for early life exposures. Otherwise, CSD does not recommend extending the default age-dependent potency adjustment factors to these carcinogenic effects. This position would be analogous to recommending a default ADAF of 1 for all lifestages.

The non-threshold approach for carcinogenicity risk assessment arises initially from the mechanistic, one-hit model, which assumes that only one-hit is required for the cell to be altered. The role of the body's defence mechanism (e.g. repair, apoptosis), which has an influence on the health outcome, is not considered. CSD considers the use of the linear low-dose extrapolation approach (without further adjustment) to be sufficiently conservative and to provide adequate public health protection for carcinogenic effects with a mode of action that is not mutagenic.

3.2 Assessment of Health Risk from Threshold Carcinogens

The CSD does not recommend a default age-specific adjustment for carcinogenic effects found to have a non-linear dose-response relationship (i.e. threshold) at low doses at this time. An adjustment can be made on a chemical-specific basis if supported by experimental data. These substances would be included in an HHRA using a TDI (or a TC in the case of inhalation exposure).

The CSD recommends that dose averaging for short-term exposure for these types of carcinogenic effects be performed in the same way as for other substances with threshold effects. It is important that dose averaging does not underestimate the potential for threshold carcinogenic effects. Without a sound basis for doing so (i.e. it cannot be a default assumption), the human health risk assessor should not simply mathematically spread out a short-term dose over a long period and conclude that the short-term dose is toxicologically equivalent to a lower dose over the long period. In short, CSD recommends that the exposure be averaged over the total actual exposure period and compared with the appropriate TRV. A scientific rationale is required to support any proposed amortization (dose averaging beyond actual exposure period) to ensure that short-term risks are not underestimated. This analysis needs to be done on a chemical-specific basis.

3.3 Assessment of Health Risk from Non-Cancer Health Effects

For short-term exposure, carcinogenic agents may elicit other chronic and short-term non-cancer health effects, depending on the magnitude of exposure. Short-term effects can be evaluated for potential critical receptors/lifestages[5] using short-term TRVs where available (either from other regulatory agencies or derived from literature values, as per Health Canada, 2010, guidance) and applicable to the exposure scenarios. If short-term TRVs are not available, such evaluation can be conducted according to relevant dose-response information from toxicity studies. It is also important to consider whether the short-term exposure might elicit early biological key events that might progress to health effects at a later date. In many cases, both the short-term and chronic non-carcinogenic effects, rather than carcinogenicity, may be the main determinant of the risk from short-term exposure. For example, keratosis rather than carcinogenicity could drive a risk assessment for exposure to high levels of arsenic in soil (e.g. 100 mg/kg) in a less-than-lifetime exposure scenario.

[5] Including relevant receptors/lifestages with the highest exposure and receptors/lifestages associated with specific sensitivity to the toxicity of the contaminants

4.0 WORKED EXAMPLES

4.1 Assessment of Lifetime Risk Associated with Exposure to a Carcinogen with a Mutagenic Mode of Action

When assessing cancer risk, it is important to consider both the difference in exposure and the increased susceptibility for early lifestages. ADAFs in dose-response (i.e. slope factors) need to be combined with age-specific exposure estimation.

The following examples illustrate how to integrate potential lifestage differences in exposure and susceptibility in risk estimation for both lifetime and less-than-lifetime exposure during a specific period in life. The examples consider risk from oral exposure. Risks associated with inhalation exposure to mutagenic carcinogens can be calculated in a similar manner by applying the appropriate ADAFs with the corresponding inhalation unit risk estimates using appropriate estimates of exposure concentrations.

These calculations assume that the available slope factor does not specifically consider early-life exposure. In the case of carcinogens for which age-specific (and in particular early-life) slope factors are available, these factors should be used instead of adjusting the adult slope factor.

4.1.1 Example 1: Exposure Occurs Over a Lifetime

Consider a scenario of exposure to a hypothetical carcinogen with a mutagenic mode of action present in drinking water. The oral slope factor derived from a typical animal study (i.e. in which dosing begins after puberty) is estimated to be 2 $(mg/kg\text{-}d)^{-1}$. The absorption factor of the carcinogen from drinking water is 1. The carcinogen is present in drinking water at 0.001 mg/L.

To calculate lifetime risk for a population with average life expectancy of 80 years, sum the risk associated with each of the time periods, applying recommended ADAFs to the relevant time periods:

- risk for the infant—first 6 months of life (where ADAF = 10),
- risk for toddler—6 months through 4 years of life (ADAF = 5),
- risk for child—ages 5 through 11 (ADAF = 3),
- risk for teenager—ages 12 through 19 (ADAF = 2) and
- risk for adult—ages 20 to 80 (ADAF = 1)

Thus, the ILCR equals the sum of the various age groups:

- Risk for infant
  = slope factor × ADAF x $LADD_{0–6\ mo}$
  = 2 $(mg/kg\text{-}d)^{-1}$ × 10 × [(0.001 mg/L × 0.3 L/d / 8.2 kg) × 0.5 yr/80yr]
  = 5 x 10^{-6}
- Risk for toddler
  = slope factor × ADAF × $LADD_{7\ mo–4}$
  = 2 $(mg/kg\text{-}d)^{-1}$ × 5 × [(0.001 mg/L × 0.6 L/d / 16.5 kg) × 4.5 yr/80yr]
  = 2 × 10^{-5}
- Risk for children
  = slope factor × ADAF × $LADD_{5–11}$
  = 2 $(mg/kg\text{-}d)^{-1}$ × 3 × [(0.001 mg/L × 0.8 L/d / 32.9 kg) × 7 yr/80yr]
  = 1 × 10^{-5}
- Risk for teenager
  = slope factor × ADAF × $LADD_{12–19}$
  = 2 $(mg/kg\text{-}d)^{-1}$ × 2 × [(0.001 mg/L × 1 L/d / 59.7 kg) × 8 yr/80yr]
  = 8 × 10^{-6}
- Risk for adult
  = slope factor × ADAF × $LADD_{20+}$
  = 2 $(mg/kg\text{-}d)^{-1}$ x 1 × [(0.001 mg/L × 1.5 L/d / 70.7 kg) × 60 yr/80yr]
  = 3 × 10^{-5}

Total ILCR
= 5 × 10^{-6} + 2 × 10^{-5} + 1 × 10^{-5} + 8 × 10^{-6} + 3 × 10^{-5}
= 7 × 10^{-5}

4.1.2 Example 2: Exposure Occurs at Less Than 2 Years of Age

Consider a scenario in which exposure to the same hypothetical carcinogen only takes place for a limited period of time, e.g. in a family that lives near a source of contamination for a short time and then moves away. The exposure may occur with a child aged from 1 to less than 2 years of age. It is important to consider lifestage-specific differences in exposure. The carcinogen has an oral cancer slope factor of 2 $(mg/kg\text{-}d)^{-1}$ derived from a typical animal study, and the concentration in drinking water is 0.001 mg/L.

As this exposure period does not match CSD age groupings, the US EPA's ADAF applies[6].

Risk = slope factor × ADAF × $LADD_{1-<2}$
Risk = 2 $(mg/kg\text{-}d)^{-1}$ × 10 × 0.001 mg/L × 0.6 L/d/16.5 kg × 1 yr/80 yrs
= 9 × 10^{-6}

Thus, the incremental lifetime cancer risk from 1 year of exposure to a carcinogen with a mutagenic mode of action assuming initial exposure at 1 year of age is estimated at 9 × 10^{-6}.

[6] Please note that when the exposure period matches a CSD age grouping, CSD recommends that its ADAFs be used.

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Exhibit G

Technical Support Document for Cancer Potency Factors:

Methodologies for derivation, listing of available values, and adjustments to allow for early life stage exposures.

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California Environmental Protection Agency

Office of Environmental Health Hazard Assessment

Air Toxicology and Epidemiology Branch

Prepared by:

John D. Budroe, Ph.D.

Joseph P. Brown, Ph.D.

James F. Collins, Ph.D.

Melanie A. Marty, Ph.D.

Andrew G. Salmon, M.A., D.Phil.

Air Toxicology and Epidemiology Branch

and

Martha S. Sandy, Ph.D., M.P.H.

Claire D. Sherman, Ph.D.

Rajpal S. Tomar, Ph.D.

Lauren Zeise, Ph.D.

Reproductive and Cancer Hazard Assessment Branch,

Office of Environmental Health Hazard Assessment

Reviewed By

George V. Alexeeff, Ph.D., Deputy Director

Melanie A. Marty, Ph.D., Chief, Air Toxicology and Epidemiology Branch

Lauren Zeise, Ph.D., Chief, Reproductive and Cancer Hazard Assessment Branch

EXECUTIVE SUMMARY

The Air Toxics "Hot Spots" Information and Assessment Act (AB 2588, Connelly) was enacted in September 1987. Under this Act, stationary sources of air pollution are required to report the types and quantities of certain substances their facilities routinely release into the air. The goals of the Air Toxics "Hot Spots" Act are to collect emission data, identify facilities having localized impacts, ascertain health risks posed by those facilities, notify nearby residents of significant risks and reduce emissions from significant sources.

The Technical Support Document for Cancer Potency Factors (TSD) contains cancer unit risks and potency factors for 107 of the 201 carcinogenic substances or groups of substances for which emissions must be quantified in the Air Toxics Hot Spots program. These unit risks are used in the cancer risk assessment of facility emissions.

The purpose of this revision to the TSD is to provide updated calculation procedures used to derive the estimated unit risk and cancer potency factors, and to describe the procedures used to consider the increased susceptibility of infants and children compared to adults to carcinogens. This updates cancer risk assessment methods originally laid out in the California Department of Health Services' Guidelines for Chemical Carcinogen Risk Assessment (CDHS, 1985), and more recently summarized in the previous Hot Spots technical support document Part II (OEHHA, 2005a). Summaries of cancer potency factors and the underlying data are provided in Appendices A and B, which are subject to ongoing updates but were not changed as part of the revision process which created this TSD.

The procedures used to consider the increased susceptibility to carcinogens of infants and children as compared to adults include the use of age-specific weighting factors in calculating cancer risks from exposures of infants, children and adolescents, to reflect their anticipated special sensitivity to carcinogens

This document is one part of the Air Toxics Hot Spots Program Risk Assessment Guidelines. The other documents originally included in the Guidelines are Part I: Technical Support Document for the Determination of Acute Toxicity Reference Exposure Levels for Airborne Toxicants; Part III: Technical Support Document for Determination of Noncancer Chronic Reference Exposure Levels; Part IV: Technical Support Document for Exposure Assessment and Stochastic Analysis; Part V: Air Toxic Hot Spots Program Risk Assessment Guidelines. As a part of the same revision process which led to production of this revised TSD on cancer potencies, the original TSDs for Acute and Chronic Reference Exposure Levels have been replaced with a new unified TSD for Acute, 8-hour and Chronic Reference Exposure Levels.

The major changes to the TSD include the following:

- Based on the OEHHA analysis of the potency by lifestage at exposure, OEHHA proposes weighting cancer risk by a factor of 10 for exposures that occur from the third trimester of pregnancy to 2 years of age, and by a factor of 3 for exposures that occur from 2 years through 15 years of age. We intend to apply this weighting factor to all carcinogens,

regardless of purported mechanism of action, unless chemical-specific data exist to the contrary. In cases where there are adequate data for a specific carcinogen of potency by age, we would use the data to make any adjustments to risk.

- OEHHA proposes to use the Benchmark Dose method to compute potency factors rather than the more traditional linearized multistage model (LMS), although the LMS will still be used in some instances. The BMDL model essentially uses an empirical fit to the data (usually best with the multistage model), and then extrapolates with a straight line from the 95% lower confidence limit of the BMD (BMDL) to zero. This method is simpler and does not assume any underlying theoretical mechanisms at the low dose range. The BMDL method results in estimates of potency very similar to those obtained using the LMS method.

- OEHHA will use scaling based on body weight to the ¾ power, rather than to the ⅔ power.

- OEHHA's evaluations of the carcinogenicity of chemicals generally follow the guidelines laid out by IARC for identification and classification of potential human carcinogens, which are described in detail in the most recent revision of the *Preamble* to the IARC monographs series (IARC, 2006).

PREFACE

The Air Toxics "Hot Spots" Information and Assessment Act (AB 2588, Connelly) was enacted in September 1987. Under this Act, stationary sources are required to report the types and quantities of certain substances their facilities routinely release into the air. The goals of the Air Toxics "Hot Spots" Act are to collect emission data, identify facilities having localized impacts, ascertain health risks posed by those facilities, notify nearby residents of significant risks and reduce emissions from significant sources.

The Technical Support Document for Cancer Potency Factors (TSD) contains cancer unit risks and potency factors for 107 of the 201 carcinogenic substances or groups of substances for which emissions must be quantified in the Air Toxics Hot Spots program. These unit risks are used in risk assessment of facility emissions. The TSD provides updated calculation procedures used to derive the estimated unit risk and cancer potency factors, and procedures to consider early-life susceptibility to carcinogens. Summaries of cancer potency factors and the underlying data are provided in Appendices A and B.

In this document, OEHHA is responding to the requirements of the 1999 Children's Environmental Health Protection Act (SB25, Escutia) by revising the procedures for derivation and application of cancer potency factors to take account of general or chemical-specific information which suggests that children may be especially susceptible to certain carcinogens (OEHHA, 2001a). The revised cancer potency derivation procedures described will not be used to impose any overall revisions of the existing cancer potencies, although they do reflect updated methods of derivation. However, individual cancer potency values will be reviewed as part of the ongoing re-evaluation of health values mandated by SB 25, and revised values will be listed in updated versions of the appendices to this document as necessary. The revisions also include the use of weighting factors in calculating cancer risks from exposures of infants, children and adolescents, to reflect their anticipated special sensitivity to carcinogens. Similar legal mandates to update risk assessment methodology and cancer potencies apply to the OEHHA program for development of Public Health Goals (PHGs) for chemicals in drinking water, and Proposition 65 No Significant Risk Levels (NSRLs). The NSRLs may also be revised to reflect concerns for children's health. Revising these numbers will require the originating program to reconsider the value in an open public process. For example, OEHHA would need to release any revised potency factors for public comment and review by the Scientific Review Panel on Toxic Air Contaminants (SRP) prior to adoption under the TAC program. The procedures for outside parties to request reevaluation of cancer potency values by the programs which originated those values are listed in Appendix G.

Appendices A and B provide previously adopted Cal/EPA values which were included in the previous version of the TSD for Cancer Potency Factors (OEHHA, 2005a). Cal/EPA values were developed under the Toxic Air Contaminant (TAC) program, the PHG program, the Proposition 65 program, or in some cases specifically for the Air Toxics Hot Spots program. All the Cal/EPA values are submitted for public comments and external peer review prior to adoption by the program of origin. In the future, new values developed by the Toxic Air Contaminants or Hot Spots programs or other suitable sources will be added as these are approved.

Some U.S. EPA IRIS cancer unit risk values were adopted under the previous versions of these guidelines, and these values will continue to be used unless and until revised by Cal/EPA. U.S. EPA has recently revised its cancer risk assessment guidelines (U.S. EPA, 2005a). Some of the recommended changes in methodology could result in slightly different potency values compared to those calculated by the previous methodology, although in practice a number of the recommendations (for example, the use of ¾ power of the body weight ratio rather than ⅔ power for interspecies scaling) have been available in draft versions of the revised policy for some time and appear in many more recent assessments. U.S. EPA has stated that cancer potency values listed in IRIS will not be revisited solely for the purpose of incorporating changes in cancer potency value calculation methods contained in the revised cancer risk assessment guidelines. U.S. EPA has also issued supplementary guidelines on assessing cancer risk from early-life exposure (U.S. EPA, 2005b).

OEHHA uses a toxic equivalency factor procedure for dioxin-like compounds, including polychlorinated dibenzo-*p*-dioxins, dibenzofurans and polychlorinated biphenyls (PCBs). The Toxicity Equivalency Factor scheme (TEF_{WHO-97}) developed by the World Health Organization/European Center for Environmental Health (WHO-ECEH) is used for determining cancer unit risk and potency values for these chemicals where individual congener emissions are available (Appendix C).

This document is one part of the Air Toxics Hot Spots Program Risk Assessment Guidelines. The other documents originally included in the Guidelines are Part I: Technical Support Document for the Determination of Acute Toxicity Reference Exposure Levels for Airborne Toxicants; Part III: Technical Support Document for Determination of Noncancer Chronic Reference Exposure Levels; Part IV: Technical Support Document for Exposure Assessment and Stochastic Analysis; Part V: Air Toxic Hot Spots Program Risk Assessment Guidelines. As a part of the same revision process which led to production of this revised TSD on cancer potencies, the original TSDs for Acute and Chronic Reference Exposure Levels have been replaced with a new unified TSD for Acute, 8-hour and Chronic Reference Exposure Levels.

TABLE OF CONTENTS

APPENDICES

Appendix A. A lookup table containing unit risk and cancer potency values.

Appendix B. Chemical-specific summaries of the information used to derive unit risk and cancer potency values.

Appendix C. A description of the use of toxicity equivalency factors for determining unit risk and cancer potency factors for polychlorinated dibenzo-*p*-dioxins, dibenzofurans and dioxin-like polychlorinated biphenyls.

Appendix D. A listing of Toxic Air Contaminants identified by the California Air Resources Board.

Appendix E. Descriptions of the International Agency for Research on Cancer (IARC) and U.S. Environmental Protection Agency (U.S. EPA) carcinogen classifications.

Appendix F. An asbestos quantity conversion factor for calculating asbestos concentrations expressed as 100 fibers/m^3 from asbestos concentrations expressed as $\mu g/m^3$.

Appendix G. Procedures for revisiting or delisting cancer potency factors by the program of origin.

Appendix H. Exposure routes and studies used to derive cancer unit risks and slope factors.

Appendix I. "Assessing susceptibility from early-life exposure to carcinogens": Barton *et al*., 2005 (from *Environmental Health Perspectives)*.

Appendix J. "In Utero and Early Life Susceptibility to Carcinogens: The Derivation of Age-at-Exposure Sensitivity Measures" – conducted by OEHHA's Reproductive and Cancer Hazard Assessment Branch.

INTRODUCTION

The Technical Support Document (TSD) for Describing Available Cancer Potency Factors provides technical information support for the Air Toxics Hot Spots Program Risk Assessment Guidelines. The TSD consists of 12 sections:

1. The TSD introduction.

2. A description of the methodologies used to derive the unit risk and cancer potency values listed in the lookup table.

3. A lookup table containing unit risk and cancer potency values. (Appendix A)

4. Chemical-specific summaries of the information used to derive unit risk and cancer potency values. (Appendix B).

5. A description of the use of toxicity equivalency factors for determining unit risk and cancer potency factors for polychlorinated dibenzo-*p*-dioxins, dibenzofurans and dioxin-like polychlorinated biphenyls (Appendix C).

6. A listing of Toxic Air Contaminants identified by the California Air Resources Board (Appendix D).

7. Descriptions of the International Agency for Research on Cancer (IARC) and U.S. Environmental Protection Agency (U.S. EPA) carcinogen classifications (Appendix E).

8. An asbestos quantity conversion factor for calculating asbestos concentrations expressed as 100 fibers/m^3 from asbestos concentrations expressed as $\mu g/m^3$ (Appendix F).

9. Procedures for revisiting or delisting cancer potency factors by the program of origin (Appendix G).

10. Exposure routes and studies used to derive cancer unit risks and slope factors (Appendix H).

11. "Assessing susceptibility from early-life exposure to carcinogens": Barton *et al*., 2005 (from *Environmental Health Perspectives)* (Appendix I).

12. "In Utero and Early Life Susceptibility to Carcinogens: The Derivation of Age-at-Exposure Sensitivity Measures" – conducted by OEHHA's Reproductive and Cancer Hazard Assessment Branch (Appendix J)

SELECTION OF CANCER POTENCY VALUES

The Office of Environmental Health Hazard Assessment (OEHHA) has developed a number of cancer potencies for use in the Toxic Air Contaminants and Air Toxics Hot Spots programs. This document also provides summaries of cancer potency factors which were originally developed for other California Environmental Protection Agency (Cal/EPA) programs, or by the U.S. EPA. These were reviewed for accuracy, reliance on up-to-date data and methodology, and applicability in the context of the Air Toxics Hot Spots program. Values found appropriate were adopted after public and peer review rather than devoting the resources necessary for a full *de novo* assessment. Thus, cancer potency values (CPF) included in the Technical Support Document (TSD) for Cancer Potency Factors were from the following sources:

1. Toxic Air Contaminant documents

2. Standard Proposition 65 documents

3. U.S.EPA Integrated Risk Information Systems (Office of Health and Environmental Assessment, U.S.EPA)

4. Expedited Proposition 65 documents

5. Other OEHHA assessments , for example for the drinking water program.

All the cancer potency value sources used generally follow the recommendations of the National Research Council on cancer risk assessment (NRC, 1983, 1994). All Cal/EPA program documents undergo a process of public comment and scientific peer review prior to adoption, although the procedures used vary according to the program. The publication procedure for Toxic Air Contaminant documents includes a public comment period and review by the Scientific Review Panel on Toxic Air Contaminants (SRP) before identification of a Toxic Air Contaminant by the Air Resources Board of the California Environmental Protection Agency (Cal/EPA). Furthermore, a petition procedure is available to initiate TAC document review and revision if appropriate because of new toxicity data. Documents developed for the Air Toxics Hot Spots program similarly undergo public comment and peer review by the SRP before adoption by the Director of OEHHA. The standard Proposition 65 document adoption procedure includes a public comment and external peer review by the Proposition 65 Carcinogen Identification Committee. The expedited Proposition 65 document adoption procedure included a public comment period. Risk assessments prepared for development of Public Health Goals (PHGs) for chemicals in drinking water are subject to two public comment periods before the final versions and responses to comments are published on the OEHHA Web site. PHG documents may also receive external peer review. Documents from U.S. EPA's Integrated Risk Information System (IRIS) receive external peer review and are posted on the Internet for public viewing during the external peer review period, and any public comments submitted are considered by the originating office. Additionally, public comment may be solicited during the document posting period. Future preference for use of developed cancer potency factors/unit risks will be done on a case by case basis. Preference will be given to those assessments most relevant to inhalation exposures of the California population, to the most recent derivations using the latest data sets and scientific methodology, and to those having undergone the most open and extensive peer review process.

CANCER RISK ASSESSMENT METHODOLOGIES

This section describes in general the methodologies used to derive the cancer unit risk and potency factors listed in this document. As noted in the Preface to this document, no new cancer unit risks or potency factors were developed for this document. All of the values contained here were previously developed in documents by Cal/EPA or U.S. EPA. Following the recommendations of the National Academy of Sciences (NRC, 1983), Cal/EPA and U.S. EPA have both used formalized cancer risk assessment guidelines, the original versions of which (California Department of Health Services, 1985; U.S. EPA, 1986) were published some time ago. Both these guidelines followed similar methodologies.

In the twenty years since these original guidelines were published there have been a number of advances in the methodology of cancer risk assessment. There have additionally been considerable advances in the quantity of data available not only from animal carcinogenesis bioassays and epidemiological studies, but also from mechanistic studies of carcinogenesis and related phenomena. Some of these advances have been incorporated into newer risk assessments by both agencies on a more or less *ad hoc* basis. There has also been an ongoing effort to provide updated risk assessment guidance documents. In 1995, U.S. EPA released for public comment the "Proposed and Interim Guidelines for Carcinogen Risk Assessment", which was the first of several drafts released for public comment. Many risk assessments appearing since then have used elements of the recommendations contained in that document, in spite of its draft status. A final version of the U.S. EPA's revised cancer risk assessment guidelines has now been released (U.S. EPA, 2005a). Although these new guidelines incorporate a number of substantial changes from their predecessors (U.S. EPA, 1986; 1995), U.S. EPA has stated that cancer potency values listed in IRIS will not be revisited solely for the purpose of incorporating changes in cancer potency value calculation methods.

Cal/EPA has not produced a revised cancer risk assessment guideline document to replace the original version (DHS, 1985). Rather, Cal/EPA has relied on incorporating new data and methodologies as these became available, and described the methods used on a case by case basis in the individual risk assessment documents where these went beyond the original guidance. However, this revision of the TSD for cancer potencies provides a convenient opportunity to summarize the current status of the methodology used by OEHHA for the air toxics programs, and also to highlight points of similarity to, and difference from, the recommendations of U.S. EPA (2005a).

In this document, OEHHA intends to follow the recommendations of the NRC (1994) in describing a set of clear and consistent principles for choosing and departing from default cancer risk assessment options. NRC identified a number of objectives that should be taken into account when considering principles for choosing and departing from default options. These include, "protecting the public health, ensuring scientific validity, minimizing serious errors in estimating risks, maximizing incentives for research, creating an orderly and predictable process, and fostering openness and trustworthiness". The OEHHA cancer risk methodologies discussed in this document are intended to generally meet those objectives cited above.

Hazard Identification

This section will describe: 1) how weight of evidence evaluations are used in hazard evaluation; 2) guidelines for inferring causality of effect; 3) the use of human and animal carcinogenicity data, as well as supporting evidence (*e.g.,* genetic toxicity and mechanistic data); 4) examples of carcinogen identification schemes.

Evaluation of Weight of Evidence

In evaluating the range of evidence on the toxicity and carcinogenicity of a compound, mixture or other agent, a "weight-of-evidence" approach is generally used to describe the body of evidence on whether or not exposure to the agent causes a particular effect. Under this approach, the number and quality of toxicological and epidemiological studies, as well as the consistency of study results and other sources of data on biological plausibility, are considered. Diverse and sometimes conflicting data need to be evaluated with respect to possible explanations of differing results. Consideration of methodological issues in the review of the toxicological and epidemiological literature is important in evaluating associations between exposure to an agent and animal or human health effects. This aspect of the evaluation process has received particular emphasis with respect to epidemiological data, where concerns as to the statistical and biological significance and reliability of the data and the impacts of confounding and misclassification are pressing. Such concerns are also relevant to some extent in the interpretation of animal bioassay data and mechanistic studies. Although the test animals, laboratory environment and characterization of the test agent are usually much better controlled than the equivalent parameters in an epidemiological study, the small sample size can be problematic. In addition, there are uncertainties associated with extrapolation of biological responses from test animal species to humans.

Criteria for Causality

There has been extensive discussion over the last two centuries on causal inference. This has particularly related to epidemiological data, but is also relevant to interpretation of animal studies. Most epidemiologists utilize causal inference guidelines based on those proposed by Bradford Hill (1971). OEHHA has relied on these and on recommendations by IARC (2006), the Institute of Medicine (2004), the Surgeon General's Reports on Smoking (U.S. DHHS, 2004) and standard epidemiologic texts (*e.g.,* Lilienfeld and Lilienfeld, 1980; Rothman and Greenland, 1998). The criteria for determination of causality used by OEHHA have been laid out in various risk assessment documents. The summary below is adapted from the Health Effects section of the document prepared to support the identification of environmental tobacco smoke (ETS) as a Toxic Air Contaminant (OEHHA, 2005b).

1. *Strength of Association*. A statistically significant strong association, which is easier to detect if there is a high relative risk, between a factor and a disease is often viewed as an important criterion for inferring causality because, all other things being equal, a strong and statistically significant association makes alternative explanations for the disease less likely. However, as discussed in Rothman and Greenland (1998), the fact that a relative risk is small in magnitude does not exclude a casual association between the risk factor and the outcome in question. Since it is more difficult to detect (*i.e.*, reach statistical

significance) a small magnitude risk, it is just as likely to indicate causality as a larger magnitude risk.

When assessing all evidence, it is important to consider the strength of the study design (particularly controlling for confounding variables, obtaining an unbiased sample, measurement error) and the level of statistical significance (*i.e.*, the ability to exclude a Type I [false positive] error). The power of the study to detect biologically meaningful effects (*i.e.*, the risk of a Type II [false negative] error) is important in considering studies that do not reach traditional (*i.e.*, $P < 0.05$) statistical significance, particularly if the biological endpoint is serious. If the outcome is serious and the study small (*i.e.*, low power), a larger P value (*e.g.*, $P < 0.10$) may be adequate evidence for identifying an effect.

There are a number of examples of statistically significant, small magnitude associations that are widely accepted as causal, such as causal links between air pollution and cardiovascular/pulmonary mortality and between second-hand smoke exposure and various cancers and heart disease. From a public health perspective, even a small magnitude increase in risk for a common disease can mean large numbers of people affected by the health outcome when exposure is frequent and widespread, as measured by the population attributable risk or attributable fraction. Small magnitude of association must not be confused with statistical significance, which is much more important.

2. *Consistency of Association.* If several investigations find an association between a factor and a disease across a range of populations, geographic locations, times, and under different circumstances, then the factor is more likely to be causal. Consistency argues against hypotheses that the association is caused by some other factor(s) that varies across studies. Unmeasured confounding is an unlikely explanation when the effect is observed consistently across a number of studies in different populations.

   Associations that are replicated in several studies of the same design or using different epidemiological approaches or considering different sources of exposure and in a number of geographical regions are more likely to represent a causal relationship than isolated observations from single studies (IARC, 2006). If there are inconsistent results among investigations, possible reasons are sought, such as adequacy of sample size or control group, methods used to assess exposure, or range in levels of exposure. The results of studies judged to be rigorous are emphasized over those of studies judged to be methodologically less rigorous. For example, studies with the best exposure assessment are more informative for assessing the association between ETS and breast cancer than studies with limited exposure assessment, all else being equal.

3. *Temporality.* Temporality means that the factor associated with causing the disease occurs in time prior to development of the disease. The adverse health effect should occur at a time following exposure that is consistent with the nature of the effect. For example, respiratory irritation immediately following exposure to an irritant vapor is temporally consistent, whereas irritation noted only years later may not be. On the other hand, tumors, noted immediately following exposure, might be temporally inconsistent with a causal relationship, but tumors arising after a latency period of months (in rodents) or years (in rodents or humans) would be temporally consistent.

4. *Coherence and Biological Plausibility.* A causal interpretation cannot conflict with what is known about the biology of the disease. The availability of experimental data or mechanistic theories consistent with epidemiological observations strengthens conclusions of causation. For example, the presence of known carcinogens in tobacco smoke supports the concept that exposure to tobacco smoke could cause increased cancer risk. Similarly, if the mechanism of action for a toxicant is consistent with development of a specific disease, then coherence and biological plausibility can be invoked. It should be noted that our understanding of the biology of disease, and therefore biological plausibility, changes in light of new information which is constantly emerging from molecular biology (including epigenetics), and from new clinical and epidemiological investigations revealing effects influenced by genetic polymorphisms, pre-existing disease, and so forth.

5. *Dose-Response.* A basic tenet of toxicology is that increasing exposure or dose generally increases the response to the toxicant. While dose-response curves vary in shape and are not necessarily always monotonic, an increased gradient of response with increased exposure makes it difficult to argue that the factor is not associated with the disease. To argue otherwise necessitates that an unknown factor varies consistently with the dose of the substance and the response under question. While increased risk with increasing levels of exposure is considered to be a strong indication of causality, absence of a graded response does not exclude a causal relationship (IARC, 2006).

   The dose-response curves for specific toxic effects may be non-monotonic. Under appropriate circumstances, where the dose response shows saturation, the effect of exposures could be nearly maximal, with any additional exposure having little or no effect. In some instances, a response is seen strongly in susceptible subpopulations, and the dose-response is masked by mixing susceptible and non-susceptible individuals in a sample. Further, there are examples of U-shaped or inverted U-shaped dose-response curves, (*e.g.*, for endocrine disrupters) (Almstrup et al., 2002; Lehmann et al., 2004). Finally, timing of exposure during development may mask an overall increase in risk with increasing dose.

6. *Specificity.* Specificity is generally interpreted to mean that a single cause is associated with a single effect. It may be useful for determining which microorganism is responsible for a particular disease, or associating a single carcinogenic chemical with a rare and characteristic tumor (*e.g.*, liver angiosarcoma and vinyl chloride, or mesothelioma and asbestos). However, the concept of specificity is not helpful when studying diseases that are multifactorial, or toxic substances that contain a number of individual constituents, each of which may have several effects and/or target sites.

7. *Experimental evidence.* While experiments are often conducted over a short period of time or under artificial conditions (compared to real-life exposures), experiments offer the opportunity to collect data under highly controlled conditions that allow strong causal conclusions to be drawn. Experimental data that are consistent with epidemiological results strongly support conclusions of causality. There are also "natural experiments" that can be studied with epidemiological methods, such as when exposure of a human population to a substance declines or ceases; if the effect attributed to that exposure decreases, then there is evidence of causality. One example of this is the drop in heart disease death and lung cancer risk after smoking cessation.

It should be noted that the causal criteria are guidelines for judging whether a causal association exists between a factor and a disease, rather than hard-and-fast rules. Lilienfeld and Lilienfeld (1980) note that "*In medicine and public health, it would appear reasonable to adopt a pragmatic concept of causality. A causal relationship would be recognized to exist whenever evidence indicates that the factors form part of the complex of circumstances that increases the probability of the occurrence of disease and that a diminution of one or more of these factors decreases the frequency of that disease. After all, the reason for determining the etiological factors of a disease is to apply this knowledge to prevent the disease.*" Rothman and Greenland (2005) discuss the complexities of causation and the use of rules and deductive methods in causal inference. They also concur with Bradford Hill and others that a determination of causality is a pragmatic conclusion rather than an absolute verdict, and advocate that these criteria should be seen as "*deductive tests of causal hypotheses".*

Data Sources

Human studies: epidemiology, ecological studies and case reports

The aim of a risk assessment for the California Air Toxics programs is to determine potential impact on human health. Ideally therefore, the hazard identification would rely on studies in humans to demonstrate the nature and extent of the hazard. However, apart from clinical trials of drugs, experimental studies of toxic effects in human subjects are rarely undertaken or justifiable. Pharmacokinetic studies using doses below the threshold for any toxic effect have been undertaken for various environmental and occupational agents, but are not usually regarded as appropriate for suspected carcinogens.

The human data on carcinogens available to the risk assessor therefore mostly consist of epidemiological studies of existing occupational or environmental exposures. It is easier to draw reliable inferences in situations where both the exposures and the population are substantial and well-defined, and accessible to direct measurement rather than recall. Thus, many important findings of carcinogenicity to humans are based on analysis of occupational exposures. Problems in interpretation of occupational epidemiological data include simultaneous exposure to several different known or suspected carcinogens, imprecise quantification of exposures and confounding exposures such as active or passive tobacco smoking. The historical database of occupational data has a bias towards healthy white adult males. Thus, the hazard analysis of these studies may not accurately characterize effects on women, infants, children or the elderly, or on members of minority ethnic groups. Nevertheless, the analysis of occupational epidemiological studies, including meta-analyses, has proved an important source for unequivocal identification of human carcinogens.

Epidemiological evidence may also be obtained where a substantial segment of a general population is exposed to the material of interest in air, drinking water or food sources. Rigorous cohort and case-control studies may sometimes be possible, in which exposed individuals are identified, their exposure and morbidity or mortality evaluated, and compared to less exposed but otherwise similar controls. More often at least the initial investigation is a cross-sectional study, where prevalence of exposures and outcomes is compared in relatively unexposed and exposed populations. Such studies are hypothesis-generating, but are important sources of information

nevertheless, and can often also justify more costly and labor-intensive follow-up cohort and/or case-control studies.

The clinical medical literature contains many case reports where a particular health outcome is reported along with unusual exposures that might have contributed to its occurrence. These reports typically describe a single patient or a small group, and have no statistical significance. They are nevertheless useful as indications of possible associations that deserve follow-up using epidemiological methods, and as supporting evidence, addressing the plausibility of associations measured in larger studies.

Animal studies

Although the observation of human disease in an exposed population can provide definitive hazard identification, adequate data of this type are not always available. More often, risk estimates have to be based on studies in experimental animals, and extrapolation of these results to predict human toxicity. The animals used are mostly rodents, typically the common laboratory strains of rat and mouse.

Rats and mice have many similarities to humans. Physiology and biochemistry are similar for all mammals, especially at the fundamental levels of xenobiotic metabolism, DNA replication and DNA repair that are of concern in identifying carcinogens. However, there are also several important differences between rodents and humans. Rodents, with a short life span, have differences in cell growth regulation compared to longer-lived species such as the human. For instance, whereas laboratory investigations have suggested that mutations in two regulatory genes (*e.g.,* H-ras and p-53) are sometimes sufficient to convert a rodent cell to a tumorigenic state, many human cancers observed clinically have seven or eight such mutations. In addition, cultured normal human cells have a very stable karyotype, whereas cultured rodent cells facilely undergo tetraploidization and then aneuploidization in cell culture. Further, cultured human cells senesce and rarely undergo spontaneous immortalization (frequency is 10^{-7} or less), whereas cultured rodent cells facilely undergo immortalization at frequencies on the order of 10^{-3}. The use of genomics to study chemical carcinogenesis is relatively new, but the differences at present appear to be a matter of degree rather than kind.

Differences in regulation of cell division are another likely reason for variation between species in the site of action of a carcinogen, or its potency at a particular site. A finding of carcinogenesis in the mouse liver, for instance, is a reasonably good indicator of potential for carcinogenesis at some site in the human, but not usually in human liver (Huff, 1999). The mouse liver (and to a lesser extent that of the rat) is a common site of spontaneous tumors. It is also relatively sensitive to chemical carcinogenesis. The human liver is apparently more resistant to carcinogenesis; human liver tumors are unusual except when associated with additional predisposing disease, such as hepatitis B or alcoholic cirrhosis, or exposure to aflatoxin B1, or simultaneous exposure to hepatitis B virus and aflatoxin B1. Conversely, other tumor sites are more sensitive in the human than in experimental animals. Interspecies variation in site and sensitivity to carcinogenesis may also arise from differences in pharmacokinetics and metabolism, especially for carcinogens where metabolic activation or detoxification is important. This variability may cause important differences in sensitivity between individuals in a diverse population such as humans. Variability

between individuals in both susceptibility and pharmacokinetics or metabolism is probably less in experimental animal strains that are bred for genetic homogeneity.

Animal carcinogenesis studies are often designed to maximize the chances of detecting a positive effect, and do not necessarily mimic realistic human exposure scenarios. Thus extrapolation from an experimentally accessible route to that of interest for a risk assessment may be necessary. Even for studies by realistic routes such as oral or inhalation, doses may be large compared to those commonly encountered in the environment, in order to counter the limitation in statistical power caused by the relatively small size of an animal experiment. Whereas the exposed population of an epidemiological study might number in the thousands, a typical animal study might have fifty individuals per exposure group. With this group size any phenomenon with an incidence of less than about 5% is likely to be undetectable. Statistically significant results may be obtained even with groups as small as ten animals per dose group, when incidence of a tumor that is rare in the controls approached 100% in a treated group. The consensus experimental design for animal carcinogenesis studies, which has evolved over the last 50 years of investigation, is represented by the protocol used by the U.S. National Toxicology Program (NTP) for studies using oral routes (diet, gavage or drinking water) or inhalation. These carcinogenesis bioassays usually involve both sexes of an experimental species, and most often two species. NTP has standardized the use of the C57BlxC3H F_1 hybrid mouse, and the Fischer 344 rat as the standard test species, although NTP has announced plans to substitute use of the Wistar Han rat for the Fischer 344 rat. There is now an extensive database of background tumor incidences, normal physiology, biochemistry, histology and anatomy for these strains, which aids in the interpretation of pathological changes observed in experiments. Nevertheless, there is enough variation in background rates of common tumors that the use of concurrent controls is essential for hazard identification or dose-response assessment. "Historical control" data are mainly used to reveal anomalous outcomes in the concurrent controls. The fact that a significantly elevated incidence of a tumor relative to the concurrent control group is within the range of historical controls at that site for the test sex and strain is not necessarily grounds for dismissing the biological significance of the finding.

Groups of fifty animals of each sex and species are used, with control groups, and several dose groups, the highest receiving the maximum tolerated dose (MTD). Recent study designs have emphasized the desirability of at least three dose levels covering a decade with "logarithmic" spacing (*i.e.* MTD, 1/2 MTD or 1/3 MTD, and 1/10 MTD). This extended design is aimed at providing better dose-response information, and may contribute important additional information, such as mechanistic insights, for the hazard identification phase.

Supporting evidence: genetic toxicity, mechanistic studies

Investigators have developed additional data sources that can support or modify the conclusions of animal carcinogenesis bioassays, and provide information on mechanisms of action of agents suspected of being carcinogenic based on epidemiological studies or animal bioassays.

Genetic damage in exposed organisms includes both gene mutations (point or frameshift), and larger scale effects such as deletions, gene amplification, sister-chromatid exchanges, translocations and loss or duplication of segments or whole chromosomes. These genetic effects of chemical exposures are deleterious in their own right. In addition, since carcinogenesis results from somatic mutations and similar genetic alterations, agents that cause genetic damage generally

have carcinogenic potential. Conversely, many known carcinogens are also known to be genotoxic, although there is also a significant class of carcinogens that are not directly genotoxic according to the usual tests. These latter agents presumably work by some other mechanism, such as methylation of tumor suppressor genes or demethylation of cellular proto-oncogenes, although recent genetic studies have shown that even tumors induced by these agents may show mutations, deletions or amplification of growth regulatory genes.

Experimental procedures to demonstrate and measure genetic toxicity may involve exposure of intact animals, and examination of genetic changes in, for example, bone marrow cells (or cells descended from these, *e.g.,* the micronucleus test, which detects remnants of chromosomal fragments in immature erythrocytes), mutations in flies (*Drosophila)*, or appearance of color spots in the coat of mice. However, many tests have employed single celled organisms or mammalian cells in culture. The best known of these tests is the *Salmonella* reverse mutation assay, popularly known as the Ames test after its inventor. This is representative of a larger class of tests for mutagenic activity in prokaryotic organisms (bacteria), which necessarily only look at gene-level mutations. Similar tests in eukaryotic microorganisms (yeasts, *Aspergillus*) and cultured mammalian cells also detect chromosomal effects. Many tests using microorganisms *in vitro* involve addition of activating enzymes (*e.g.,* liver postmitochondrial supernatant – "S9") to mimic the metabolism of promutagenic chemicals *in vivo*. Another type of test examines the induction in mammalian cells of morphological transformation or anchorage-independent growth. These two chemically induced, *in vitro* changes are considered two of the many changes that fibroblastic cells must undergo on their route to neoplastic transformation (tumorigenicity). These various genetic tests contribute different information, which may be used to amplify and confirm conclusions drawn from human studies or animal bioassays, or to draw conclusions in the absence of epidemiological or bioassay data. In the latter case they have also been used in prioritizing agents for further evaluation by means of bioassays.

Carcinogen Identification Schemes

Some regulatory programs, such as California's Safe Drinking Water and Toxics Enforcement Act ("Proposition 65") and various activities of the U.S. EPA, require that explicit lists of substances having the potential to act as human carcinogens be maintained. Other such lists are developed by non-regulatory research organizations, such as the U.S. National Toxicology Program and the International Agency for Research on Cancer (IARC), an international program of the World Health Organization. The California air toxics programs do not have any statutory requirement to "identify" carcinogens. The requirement instead is to identify hazardous substances as Toxic Air Contaminants, and to determine whether or not a threshold concentration, below which no adverse effects are expected, is likely to exist:

> ***HEALTH AND SAFETY CODE, Division 26 (Air Resources), § 39660.***
>
> *(2) The evaluation shall also contain an estimate of the levels of exposure that may cause or contribute to adverse health effects. If it can be established that a threshold of adverse health effects exists, the estimate shall include both of the following factors:*
>
> *(A) The exposure level below which no adverse health effects are anticipated.*

> *(B) An ample margin of safety that accounts for the variable effects that heterogeneous human populations exposed to the substance under evaluation may experience, the uncertainties associated with the applicability of the data to human beings, and the completeness and quality of the information available on potential human exposure to the substance. In cases in which there is no threshold of significant adverse health effects, the office shall determine the range of risk to humans resulting from current or anticipated exposure to the substance.*

In practice however this requirement amounts to the need to establish whether or not a substance is carcinogenic. Any such effects are clearly harmful. Whereas the great majority of non-cancer health effects of chemicals are regarded as having a threshold, the default assumption for carcinogens is that there is no threshold (as described below). OEHHA follows the guidelines laid out by IARC for identification and classification of potential human carcinogens, which are described in detail in the most recent revision of the *Preamble* to the IARC monographs series (IARC, 2006). The IARC Monograph series provides evaluations of the carcinogenicity of individual substances or commonly occurring mixtures. The evaluation guidelines used are similar to those used by other scientific or regulatory authorities, including U.S.EPA.

The data inputs to hazard identification for carcinogens are human epidemiological studies, animal bioassays, along with supporting evidence such as mechanistic and genotoxicity data and structure-activity comparisons. IARC also assembles data on the structure and identity of the agent. The list of agents considered includes specific chemicals and also complex mixtures, occupational and lifestyle factors, physical and biological agents, and other potentially carcinogenic exposures.

IARC evaluations determine the quality of evidence for both animal and human evidence as falling into one of four categories: sufficient evidence of carcinogenicity, limited evidence of carcinogenicity, inadequate evidence of carcinogenicity and evidence suggesting lack of carcinogenicity. Stringent requirements for data quality are imposed. In view of their crucial importance, these definitions are quoted directly from the *Preamble* (IARC 2006):

> **"(a) Carcinogenicity in humans**
>
> ***Sufficient evidence of carcinogenicity:*** The Working Group considers that a causal relationship has been established between exposure to the agent and human cancer. That is, a positive relationship has been observed between the exposure and cancer in studies in which chance, bias and confounding could be ruled out with reasonable confidence. A statement that there is *sufficient evidence* is followed by a separate sentence that identifies the target organ(s) or tissue(s) where an increased risk of cancer was observed in humans. Identification of a specific target organ or tissue does not preclude the possibility that the agent may cause cancer at other sites.
>
> ***Limited evidence of carcinogenicity*:** A positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.
>
> ***Inadequate evidence of carcinogenicity:*** The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence

of a causal association between exposure and cancer, or no data on cancer in humans are available.

Evidence suggesting lack of carcinogenicity: There are several adequate studies covering the full range of levels of exposure that humans are known to encounter, which are mutually consistent in not showing a positive association between exposure to the agent and any studied cancer at any observed level of exposure. The results from these studies alone or combined should have narrow confidence intervals with an upper limit close to the null value (*e.g.,* a relative risk of 1.0). Bias and confounding should be ruled out with reasonable confidence, and the studies should have an adequate length of follow-up. A conclusion of *evidence suggesting lack of carcinogenicity* is inevitably limited to the cancer sites, conditions and levels of exposure, and length of observation covered by the available studies. In addition, the possibility of a very small risk at the levels of exposure studied can never be excluded.

(b) Carcinogenicity in experimental animals

Carcinogenicity in experimental animals can be evaluated using conventional bioassays, bioassays that employ genetically modified animals, and other in-vivo bioassays that focus on one or more of the critical stages of carcinogenesis. In the absence of data from conventional long-term bioassays or from assays with neoplasia as the end-point, consistently positive results in several models that address several stages in the multistage process of carcinogenesis should be considered in evaluating the degree of evidence of carcinogenicity in experimental animals.

The evidence relevant to carcinogenicity in experimental animals is classified into one of the following categories:

***Sufficient evidence of carcinogenicity*:** The Working Group considers that a causal relationship has been established between the agent and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms in (a) two or more species of animals or (b) two or more independent studies in one species carried out at different times or in different laboratories or under different protocols. An increased incidence of tumours in both sexes of a single species in a well-conducted study, ideally conducted under Good Laboratory Practices, can also provide *sufficient evidence*.

A single study in one species and sex might be considered to provide *sufficient evidence of carcinogenicity* when malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumour or age at onset, or when there are strong findings of tumours at multiple sites.

***Limited evidence of carcinogenicity*:** The data suggest a carcinogenic effect but are limited for making a definitive evaluation because, *e.g.,* (a) the evidence of carcinogenicity is restricted to a single experiment; (b) there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the studies; (c) the agent increases the incidence only of benign neoplasms or lesions of uncertain neoplastic potential; or (d) the evidence of carcinogenicity is restricted to studies that demonstrate only promoting activity in a narrow range of tissues or organs.

***Inadequate evidence of carcinogenicity*:** The studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect because of major qualitative or quantitative limitations, or no data on cancer in experimental animals are available.

***Evidence suggesting lack of carcinogenicity*:** Adequate studies involving at least two species are available which show that, within the limits of the tests used, the agent is not carcinogenic. A conclusion of *evidence suggesting lack of carcinogenicity* is inevitably limited to the species, tumour sites, age at exposure, and conditions and levels of exposure studied."

IARC utilizes the evaluations of animal and human data, along with supporting evidence including genotoxicity, structure-activity relationships, and identified mechanisms, to reach an overall evaluation of the potential for carcinogenicity in humans. The revised *Preamble* (IARC, 2006) includes a description of the data evaluation criteria for this supporting evidence, and indications as to the situations where the availability of supporting evidence may be used to modify the overall conclusion from that which would be reached on the basis of bioassay and/or epidemiological evidence alone. The overall evaluation is expressed as a numerical grouping, the categories of which are described below, as before by directly quoting IARC (2006):

"Group 1: The agent is *carcinogenic to humans*.

This category is used when there is *sufficient evidence of carcinogenicity* in humans. Exceptionally, an agent may be placed in this category when evidence of carcinogenicity in humans is less than *sufficient* but there is *sufficient evidence of carcinogenicity* in experimental animals and strong evidence in exposed humans that the agent acts through a relevant mechanism of carcinogenicity.

Group 2.

This category includes agents for which, at one extreme, the degree of evidence of carcinogenicity in humans is almost *sufficient*, as well as those for which, at the other extreme, there are no human data but for which there is evidence of carcinogenicity in experimental animals. Agents are assigned to either Group 2A (*probably carcinogenic to humans*) or Group 2B (*possibly carcinogenic to humans*) on the basis of epidemiological and experimental evidence of carcinogenicity and mechanistic and other relevant data. The terms *probably carcinogenic* and *possibly carcinogenic* have no quantitative significance and are used simply as descriptors of different levels of evidence of human carcinogenicity, with *probably carcinogenic* signifying a higher level of evidence than *possibly carcinogenic*.

Group 2A: The agent is *probably carcinogenic to humans*.

This category is used when there is *limited evidence of carcinogenicity* in humans and *sufficient evidence of carcinogenicity* in experimental animals. In some cases, an agent may be classified in this category when there is *inadequate evidence of carcinogenicity* in humans and *sufficient evidence of carcinogenicity* in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans. Exceptionally, an agent may be classified in this category solely on the basis of *limited*

evidence of carcinogenicity in humans. An agent may be assigned to this category if it clearly belongs, based on mechanistic considerations, to a class of agents for which one or more members have been classified in Group 1 or Group 2A.

Group 2B: The agent is *possibly carcinogenic to humans*.

This category is used for agents for which there is *limited evidence of carcinogenicity* in humans and less than *sufficient evidence of carcinogenicity* in experimental animals. It may also be used when there is *inadequate evidence of carcinogenicity* in humans but there is *sufficient evidence of carcinogenicity* in experimental animals. In some instances, an agent for which there is *inadequate evidence of carcinogenicity* in humans and less than *sufficient evidence of carcinogenicity* in experimental animals together with supporting evidence from mechanistic and other relevant data may be placed in this group. An agent may be classified in this category solely on the basis of strong evidence from mechanistic and other relevant data.

Group 3: The agent is *not classifiable as to its carcinogenicity to humans*.

This category is used most commonly for agents for which the evidence of carcinogenicity is *inadequate* in humans and *inadequate* or *limited* in experimental animals.

Exceptionally, agents for which the evidence of carcinogenicity is *inadequate* in humans but *sufficient* in experimental animals may be placed in this category when there is strong evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans.

Agents that do not fall into any other group are also placed in this category.

An evaluation in Group 3 is not a determination of non-carcinogenicity or overall safety. It often means that further research is needed, especially when exposures are widespread or the cancer data are consistent with differing interpretations.

Group 4: The agent is *probably not carcinogenic to humans*.

This category is used for agents for which there is *evidence suggesting lack of carcinogenicity* in humans and in experimental animals. In some instances, agents for which there is *inadequate evidence of carcinogenicity* in humans but *evidence suggesting lack of carcinogenicity* in experimental animals, consistently and strongly supported by a broad range of mechanistic and other relevant data, may be classified in this group."

The IARC hazard evaluation system provides a detailed and generally accepted scheme to classify the strength of evidence as to the possible human carcinogenicity of chemicals and other agents. This includes careful consideration of mechanistic data and other supporting evidence, the evaluation of which is also important to inform selection of models or defaults used in dose response assessment, as is described below. The extended consideration of supporting evidence is in fact the primary difference between more recent versions of the guidance from IARC, and also by other organizations including U.S. EPA, and the original versions of that guidance. In fact, the basic criteria for hazard identification based on bioassay and epidemiological data have not

changed substantially in other respects from earlier guidance documents, including that originally published by California (DHS, 1985). Although as noted earlier the California Air Toxics programs do not categorize identified carcinogens, it has generally been the practice to regard any agent with an IARC overall classification in Group 1 or Group 2 as a known or potential human carcinogen. This implies the selection of various policy-based default options, including absence of a threshold in the dose-response curve, unless specific data are available to indicate otherwise. The same basic identification criteria are used by OEHHA scientific staff to determine the appropriate treatment of agents not evaluated by IARC, or for which newer data or revised interpretations suggest that an earlier IARC determination is no longer appropriate.

U.S. EPA has also proposed a scheme for carcinogen hazard identification and strength of evidence classification in their recently finalized Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005). These principally differ from the IARC guidance in recommending a more extensive narrative description rather than simply a numerical identifier for the identified level of evidence, and also to some degree in the weight accorded to various types of supporting evidence. However, for most purposes they may be regarded as broadly equivalent to the scheme used by IARC, and OEHHA has chosen to cite the IARC (2006) *Preamble* as representing the most up-to-date and generally accepted guidance on this issue.

Dose Response Assessment

The dose-response phase of a cancer risk assessment aims to characterize the relationship between an applied dose of a carcinogen and the risk of tumor appearance in a human. This is usually expressed as a cancer slope factor ["potency" – in units of reciprocal dose - usually $(mg/kg\text{-}body\ weight.day)^{-1}$ or "unit risk" – reciprocal air concentration – usually $(\mu g/m^3)^{-1}$] for the lifetime tumor risk associated with lifetime continuous exposure to the carcinogen at low doses. Cancer potency factors may also be referred to as "cancer slope factors". (As will be described later, additional algorithms may need to be applied to determine risk for specific age groups, or at higher doses where toxicokinetic factors have significant effect.) The basic methodologies recommended in this document are similar to those described by U.S. EPA (2005a) in their Carcinogen Risk Assessment Guidelines. This document therefore refers to U.S. EPA (2005a) for explanation of detailed procedures, and will provide only a brief summary except in cases where OEHHA recommendations are different from or more explicit than those of U.S. EPA.

The following descriptions of methods for dose response assessment, and considerations in their application, apply in principle to the analysis of both animal and human (epidemiological) cancer incidence data. Indeed, the original formulation of the multistage model (Armitage and Doll, 1954) described below was developed based on human cancer incidence. Nevertheless, the number and quality of human cancer incidence datasets are limited. The more complex analyses have usually only been possible for animal experimental data, where the interindividual variability and the exposure conditions can be both measured and controlled. Most commonly, epidemiological studies have necessarily used a form of multivariate analysis to separate the effects of several different variables relating to exposure, demographics and behaviors (*e.g.,* smoking). In these analyses it is usually assumed that the effect measure(s) vary linearly with the exposure: any more complex variance assumptions might exceed the power of the data to determine the required model parameters. However, there are exceptions, especially for occupational studies where the critical exposure is measured as a continuous variable (rather than

just categorical) and where the effect of this exposure is substantial relative to other confounding factors. For example, OEHHA (1998) used a multistage model dealing with both exposure intensity and duration in the analysis of cancer incidence in railroad workers exposure to diesel exhaust (Garshick et al., 1988)

Interspecies Extrapolation

The procedures used to extrapolate low-dose human cancer risk from epidemiological or animal carcinogenicity data are generally health-protective in that they determine an upper confidence bound on the risk experienced by an exposed population. As statistical estimates they cannot be regarded as definite predictions of the risk faced by any one specific individual, who might for a variety of reasons, including individual exposure and susceptibility, experience a risk different from the estimate. The risk assessment procedures used aim to include the majority of variability in the general human population within the confidence bounds of the estimate, although the possibility that some individuals might experience either lower or even no risk, or a considerably higher risk, cannot be excluded. Additionally, differences may exist between the characteristics of the general public and those of studied populations. For example, healthy workers, the subject of most epidemiological studies, are often found to have lower rates of morbidity and mortality than the general population (Wen et al., 1983; Monson, 1986; Rothman and Greenland, 1998). Most human data are derived from studies of largely male adult workers and risk estimates cannot take into account specific physiological factors of women, children, and older populations that may affect the potency of a carcinogen, including early age-at-exposure.

Dose-response assessment based on environmental epidemiological studies may involve evaluation of health impacts at exposure levels within the range of those measured in the study population. However, more usually the source data are studies of occupationally exposed humans or of animals, in which case the exposures in the study are likely to be much higher than those of concern for risk assessments relating to community or ambient exposures. Further, even when extrapolation from animal species to humans is not required, the general population to which the URF is applied may differ in characteristics relative to the occupational population studied. It is therefore necessary to extrapolate from the available data to the population and exposure range of concern, which is done by using a dose-response model derived from the source data. The models used fall into three main classes: mechanistically based models, empirical models and (where data are lacking to support a true data-based model) default assumptions. The factors affecting the dose-response relationships for carcinogenesis may also be divided into those relating to absorption, distribution, metabolism and excretion on the one hand (*i.e.* toxicokinetics), and those relating to the underlying dose-response characteristics of carcinogenesis at the tissue or cellular level (*i.e.* toxicodynamics). In this sense the problem of dose response assessment for carcinogens is similar to that for non-cancer toxic effects. The toxicokinetic models used may in fact be similar for both situations, but the toxicodynamic models are generally different.

Intraspecies Extrapolation and Inter-individual Variability

In estimating the impact of a particular level of exposure to a carcinogen on a target human population, it is necessary to consider the range of susceptibility in the target population. In the present case this is typically defined as the general population of the State of California, including of course women (some of whom are pregnant), infants and children, the elderly, the sick, and

those with genetic polymorphisms or acquired differences which affect their susceptibility to carcinogens. In general it has been assumed that the upper-bound risk estimates obtained from the standard toxicodynamic models described below are sufficiently health-protective to cover the intrinsic variability of the adult human target population, in spite of the fact that these models do not explicitly address this type of variability, except in the few cases where an estimate is based on epidemiological data from a large and unselected study group (U.S. EPA, 2005a). However, various analyses (Drew et al., 1983; Barton et al., 2005; Appendix J) have suggested that this assumption is inadequate to cover the expected variability within a human population that includes infants and children. Accordingly both U.S. EPA (2005b) and this document now offer guidance on the use of age-specific adjustment factors to allow for the potentially greater sensitivity of infants and children to chemical carcinogenesis.

The ability to accommodate human variability with regard to the toxicokinetic factors affecting susceptibility to carcinogens varies with the level of detail used in the particular assessment. If the generic interspecies extrapolation approach based on body weight is used without any explicit toxicokinetic model, then the assumption is made, as in the case of toxicodynamic variability, that the overall health-protective assumptions made are sufficient to cover the toxicokinetic variability. On the other hand if explicit models such as those referenced in the following paragraph are used, this variability may be more explicitly accommodated by using parameter values which are taken as point estimates from measured distributions of population values, or by using Monte Carlo techniques to include those distributions in the model (Bois et al., 1996; OEHHA, 1992; 2001b).

Toxicokinetic Models

Considerable literature exists showing the importance of understanding the toxicokinetics of carcinogens in understanding their mechanism of action, sites of impact and dose-response relationships. U.S. EPA (2005) in Section 3.1 refers to the importance of identifying an appropriate dose metric for the dose-response analysis. Early cancer risk assessments typically used applied dose as the dose metric, which is adequate in simple cases provided appropriate correction factors are applied for interspecies extrapolation. However, it is often observed that the uptake, metabolism and elimination of the carcinogenic substance (and/or a procarcinogen and metabolites) is non-linear, especially at the higher doses employed in experimental animal studies (Hoel *et al*., 1983, Gaylor *et al*., 1994). Extrapolation to lower doses where such relationships tend to linearity (Hattis, 1990) is aided by the use of toxicokinetic models. These may be relatively simple compartment models, or sophisticated "physiologically based pharmacokinetic (PBPK) models" which to a greater or lesser degree model the actual biochemical and physiological events of toxicokinetic importance. Applications of both types of model may be found in various risk assessment documents prepared for the Toxic Air Contaminants program (and other OEHHA risk assessments). Since the details vary widely according to the nature of the chemical and the availability of appropriate kinetic data these general guidelines will defer to those examples rather than attempt a fuller exposition here. Further analysis of the use of toxicokinetic modeling in extrapolation from animals to humans, and in accounting for interindividual variability among adult humans, infants and children is presented in the Air Toxics Hot Spots *Technical Support Document for the Derivation of Noncancer Reference Exposure Levels* (OEHHA, 2008). Although this refers to the use of toxicokinetic modeling in non-cancer risk assessment, the primary considerations are similar for cancer risk assessment.

Toxicodynamic Models

An early use of mechanistic analysis to support risk assessment was the development of the Armitage-Doll multistage model of dose-response for carcinogenesis. The multistage model was initially developed on theoretical grounds, and by examination of epidemiological and animal data on time to tumor incidence. Subsequent discovery of the molecular biology of proto-oncogenes has provided a basis for explaining the model in terms of actual biological events and systems (Barrett and Wiseman, 1987). This model was developed by Crump and others into the "linearized multistage model", which has been extensively used for carcinogen risk assessment. It leads to a number of partially verifiable predictions, including linearity of the dose-response relationship at low doses, which is observed for many genotoxic carcinogens. It also predicts the form of the dose-response relationship at higher doses, which generally follow a polynomial form (subject to sampling and background corrections) except where other identifiable factors such as pharmacokinetics intervene.

It has been argued that the simple linearized form of the multistage model has limitations as a description of carcinogenic mechanisms, which detract from its usefulness and generality. Cell proliferation is known to be important in the progression of cancer. It may actually be the primary mechanism of action for a few carcinogens, as opposed to the direct modification of DNA by the carcinogen or a metabolite which is assumed to cause the mutational event at each stage in the original multistage description. A cell proliferation model has been developed (Moolgavkar and Knudson, 1981), which retains the concept of an initiating mutational event (in most cases caused by interaction of the chemical with DNA, although it could also be a spontaneous mutation) as in the original multistage model, but also considers proliferation, death or terminal differentiation of both normal and initiated cells. This model is thought to better describe the biological events in carcinogenesis. However, it has not been used extensively in risk assessment because it requires many parameters that are difficult to define and measure (such as proliferation and death rates for various classes of cell). If these cannot be accurately determined, the model has too many free parameters and is not helpful in defining extrapolated values for risk assessment purposes. This highlights a general problem in using mechanistic models in carcinogen risk assessment, which is that the carcinogenesis data themselves are generally insufficient to define fully the dose response curve shape at low doses or provide much mechanistic information. The analysis is therefore supplemented with policy-based assumptions (such as the expectation of linearity at low doses) and, wherever possible, additional experimental measurements relating to the mechanism of action, in order to make meaningful prediction of risk from environmental exposures to humans.

Because of the difficulties in validating simplified mechanistic models such as the basic multistage model, and the additional difficulty of parameter estimation with more complex mechanistic models, the new U.S. EPA guidelines (U.S. EPA, 2005a) and some recent California risk assessments have chosen instead to use a less overtly mechanistic approach. This approach combines benchmark dose methodology (described below) with an explicit choice of the method for low-dose extrapolation, either assuming low-dose linearity or, for certain carcinogens where data indicate that this is appropriate, a "margin of exposure" or safety/uncertainty factor based approach. This benchmark method is now normally recommended for carcinogen dose response analysis, and the results generally differ little from those derived by the linearized multistage model. Although the linearized multistage method is no longer recommended as the default approach for cancer potency estimation it remains a plausible alternative in many cases, and still

has useful applications, such as for time-to-tumor analyses for which benchmark methods are not yet widely available. Additionally, a considerable number of existing cancer potencies in Appendices A and B, and used in the Air Toxics Hot Spots program were derived by this method. Many of these would not be significantly different if calculated by the benchmark approach, and are unlikely to be replaced soon by newly calculated values. The linearized multistage method will therefore also be briefly described here.

Benchmark Dose Methodologies

The use of benchmark dose methodology has been explored by various investigators [including Gaylor et al. (1998); van Landingham et al. (2001) and Crump (1984, 1995, 2002)] as a tool for dose response extrapolation. This has been recommended in regulatory guidelines for both carcinogenic (U.S. EPA, 2005a) and non-carcinogenic (U.S. EPA, 1995) endpoints. The basic approach is to fit an arbitrary function to the observed incidence data, and to select a "point of departure" (POD) (benchmark dose) *within the range of the observed data.* From this a low dose risk estimate or assumed safe level may be obtained by extrapolation, using an assumed function (usually linear) or by application of uncertainty factors. The critical issue here is that no assumptions are made about the nature of the underlying process in fitting the data. The assumptions about the shape of the dose response curve (linear, threshold, etc.) are explicitly confined to the second step of the estimation process, and are chosen on the basis of policy, mechanistic evidence or other supporting considerations. The benchmark chosen is a point at the low end of the observable dose-response curve. Usually a dose at which the incidence of the tumor is 10% is chosen for animal studies, although lower effect levels may be appropriate for large epidemiological data sets. Because real experimental data include variability in the response of individual subjects, and measurement errors, likelihood methodology is applied in fitting the data. A lower confidence bound (usually 95%) of the effective dose (LED_{10}), rather than its maximum likelihood estimate (MLE), is used as the point of departure. This properly reflects the uncertainty in the estimate, taking a cautious interpretation of highly variable or error-prone data. It also reflects the instability of MLE values from complex curve-fitting routines, which has been recognized as a problem also with the linearized multistage model.

For cancer dose-response estimation using the benchmark dose method, either animal bioassay data or epidemiological data provide a suitable basis. In the absence of a pharmacokinetic model (which could provide tissue-specific dose metrics), the potency would ordinarily be based on the time-weighted average exposure during the exposure or dosing period. The model used to fit the data can be chosen from a range of available alternative quantal models, depending on which provides the best fit to the data in the observable range. In practice, the multistage polynomial fit developed for the linearized multistage model works well for most tumor data sets. Here it is being used merely as a mathematical curve-fitting tool, where the model well fits the data set, without making assumptions about its validity as a biological model of carcinogenesis.

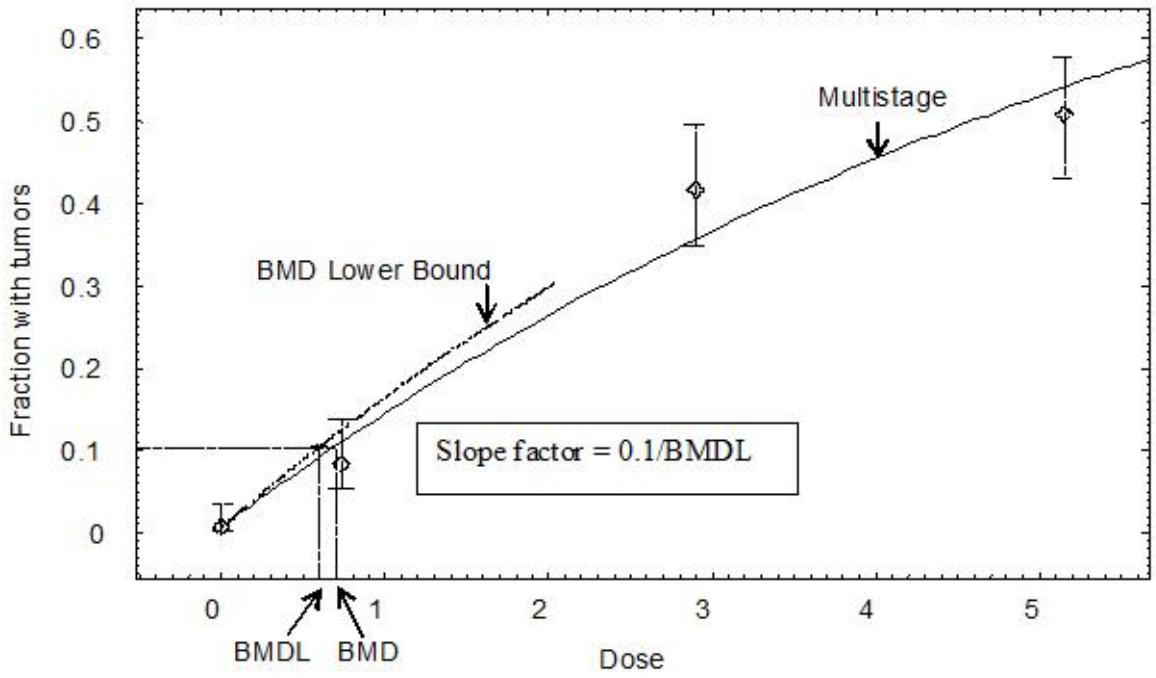
Suitable polynomial fits and estimates of the benchmark may be obtained using U.S. EPA's BMDS software. The benchmark often used is the 95% lower confidence bound on the dose producing 10% tumor incidence. However, if data are available which include a significant dose-response at less than 10% tumor incidence, then that lower benchmark should be used (*e.g.,* LED_{05} or LED_{01}). Other software such as Tox_Risk, which was used for the linearized multistage model, has been

used successfully, although the earlier GLOBAL program and its relatives are less suitable as curve-fitting tools for benchmark dose analysis.

Since it is usually assumed in cancer risk estimation that the low-dose response relationship is linear, risk estimates and a potency value (slope factor) may be obtained by linear extrapolation from an appropriate benchmark dose. The potency is the slope of that line ($0.1/LED_{10}$). The low dose linearity assumption is a general default for any carcinogen, and it is unlikely to be altered for genotoxic carcinogens.

A calculation using the benchmark dose approach (using a polynomial model with exponents restricted to zero or positive values), and linear extrapolation from the LED_{10} to obtain a potency estimate is shown in Figure 1 (the figure was generated by the U.S. EPA's BMDS program). This is based on tumor incidence data from an actual experiment with vinyl bromide in rats (Benya *et al*., 1982), with metabolized dose calculated by means of a pharmacokinetic model (Salmon *et al.,* 1992). The value of q_1* obtained by this calculation would then be corrected for the duration of the experiment if it had lasted for less than the standard rat lifetime, and for bodyweight and route-specific pharmacokinetic factors as described below. This is in addition to the correction for exposure duration that would be necessary if the study had not lasted for 105 weeks, and the interspecies correction, both of which are described below.

Figure 1. Benchmark dose calculation for tumor data in rats exposed to vinyl bromide



From Salmon *et al*. (1992), based on data from Benya *et al*. (1982)

Linearized Multistage Model

Quantal Analyses

A "multistage" polynomial (U.S. EPA, 1986, 2005a; Anderson *et al.*, 1983), based on the mechanistic insights of the original Armitage and Doll model of cancer induction and progression, has been used extensively by U.S. EPA, OEHHA and other risk assessors to model the dose response for lifetime risk of cancer. It usually is used for analysis of animal bioassay data, although related approaches have occasionally been used with epidemiological data. In mathematical terms, the probability of dying with a tumor (P) induced by an average daily dose (d) is:

$$P(d) = 1 - \exp[-(q_0 + q_1 d + q_2 d^2 + \ldots + q_j d^j)]$$

with constraints

$$q_i \geq 0 \text{ for all } i.$$

Equivalently, $$A(d) = 1 - \exp\left[- (q_1 d + q_2 d^2 + \cdots + q_k d^k)\right],$$

where $$A(d) = \frac{P(d) - P(0)}{1 - P(0)}$$ is the extra risk over background at dose d.

The q_i model parameters are constants that can be estimated by fitting the polynomial to the data from the bioassay, *i.e.* the number of tumor bearing animals (as a fraction of the total at risk) at each dose level, including the controls. The fit is optimized using likelihood methodology, assuming that the deviations from expected values follow a χ^2 distribution, with the number of degrees of freedom (and hence the maximum number of terms allowed in the polynomial) determined by the number of points in the data set. All the coefficients of the terms are constrained to be zero or positive, so the curve is required to be straight or upward curving, with no maxima, minima or other points of inflection. In addition to the maximum likelihood estimates of the parameters, the upper 95% confidence limits on these parameters are calculated.

The parameter q_0 represents the background lifetime incidence of the tumor. The 95% upper confidence limit of the slope factor q_1 (q_1^*), is termed the cancer potency. The maximum likelihood estimate (MLE) of q_1 is not usually regarded as a reliable estimate for several reasons. First, it fails to reflect the uncertainty and variability in the data which affect the value of the estimate. This is an important issue for protection of public health, which is emphasized by current regulatory guidelines. Secondly, due to the variable order of the polynomial and the effect of some terms being zero as opposed to having a small but finite value, the MLE is unstable, and may show large and unpredictable changes in response to very slight changes in the input data. It may also erratically have a zero value, even when the data imply a significant positive dose-response relationship. The MLE is not a measure of central tendency for this estimate distribution (which is always asymmetrical and often multi-peaked). For small doses, the cancer potency is the ratio of excess lifetime cancer risk to the average daily dose received. Details of the estimation procedure are given in Crump (1981) and Crump, Guess, and Deal (1977). Several software programs are available to perform the necessary calculations, including U.S. EPA's BMDS, Tox_Risk and the earlier GLOBAL programs by Crump and colleagues, and Mstage, written by Crouch (1987).

When dose is expressed in units of mg/kg-d, the potency is given in units of $(mg/kg\text{-}d)^{-1}$. Likewise, when the model input is in units of concentration ($\mu g/m^3$, ppb), the potency is given in units of $\mu g/m^3)^{-1}$ pr $(ppb)^{-1}$. As in the case of potencies obtained by the benchmark approach, the experiment-based potency value needs to be corrected for less-than lifetime or intermittent exposure, and extrapolated from the test species to humans. Risk calculations using potency value estimated using the linearized multistage model predict the cancer risk at low doses only, with the higher order terms of the fitted polynomial being ignored since their contribution is negligible at low doses.

Selection of Site and Tumor Type

In developing cancer potency estimates from animal data, standard practice has been to use dose-response data for the most sensitive tumor site as the basis of the estimate (CDHS, 1985). Where tumors of more than one histological type (*e.g.,* adenomas and carcinomas) are observed at a single

site, the combined incidence, *i.e.* proportion of animals affected with at least one tumor of any of the relevant types, is used for dose-response assessment. The same rules for combining tumor types are generally applied in determining statistical significance for carcinogen identification (IARC, 2006). Tumor types considered to represent different stages of progression following initiation of a common original normal cell type are combined, whereas tumor types having different cellular origins are generally not combined by this procedure. Other considerations that may influence choice of site for dose response estimation include the quality of the data (especially, the statistical impact of a high or variable rate of a particular tumor type and site in control animals), and biological relevance to humans. However, it is an important principle that, just as for the hazard identification phase, concordance of site or tumor type between animal models and human health effects may occur but is not assumed or required.

Carcinogens Inducing Tumors at Multiple Sites

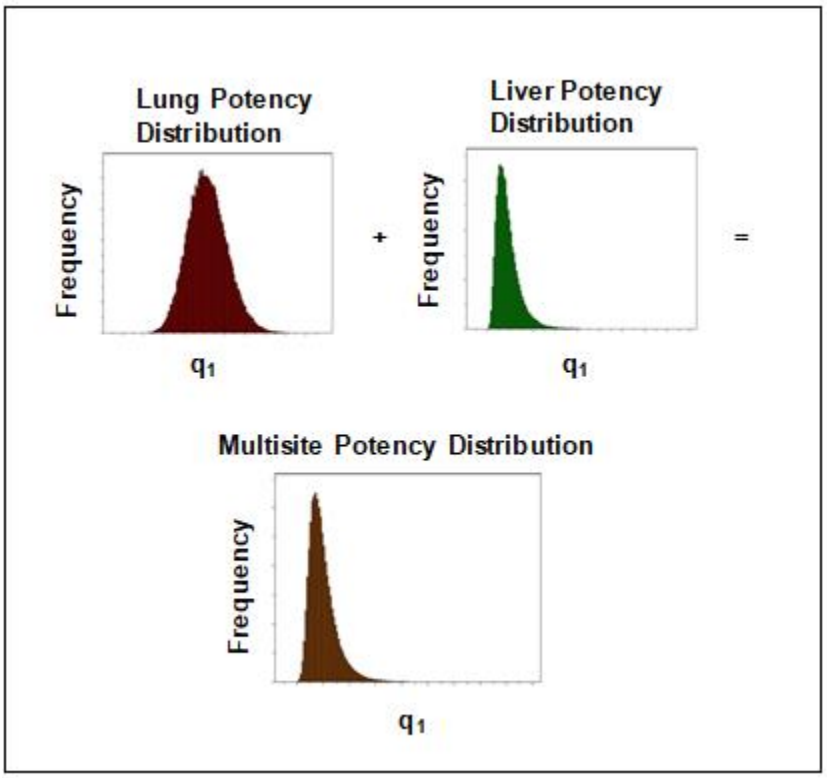
For most carcinogens, the selection of the most sensitive site in the animal studies is recognized as providing a risk estimate which is appropriate to protect human health. However, for chemicals that induce tumors at multiple sites, the single-site approach may underestimate the true carcinogenic potential. For example, the overall assessment of cancer risk from cigarette smoking (U.S. DHHS, 1982) or ionizing radiation (NRC, 1990) is not based on risk at one site, such as lung cancer. Instead, total cancer risk is estimated from all the sites at which agent-induced tumors are observed (lung, bladder, leukemia, etc), combined.

For carcinogens that induce tumors at multiple sites and/or with different cell types in a particular species and sex, OEHHA derives the animal cancer potency by probabilistically summing the potencies from the different sites and/or cell types. Using the combined potency distribution takes into account the multisite tumorigenicity and provides a basis for estimating the cumulative risk of all treatment-related tumors.

The linear term (q_1) of either the multistage model or the multistage-in-dose, Weibull-in-time model is first estimated based on the dose-response data for each of the treatment-related tumor sites. Statistical distributions, rather than point estimates, are generated at each site by tracing the profile likelihood of the linear term (q_1) (Zeise et al., 1991). The distributions of q_1 for each of the treatment-related sites are then statistically summed using a Monte Carlo approach and assuming independence (Figure 2). The sum is created by adding the linear term for each tumor site, according to its distribution, through random sampling. The upper 95 percent confidence limit on the summed distribution is taken as the multisite animal cancer potency estimate (McDonald et al., 2003, McDonald and Komulainen, 2005).

OEHHA has applied this approach in several recent dose-response analyses, including that for naphthalene presented in Appendix B of this document.

Figure 2. Addition of potency distributions for multi-site cancer potency derivations.



Early-Lifestage Cancer Potency Adjustments

In recent years, there have been growing concerns regarding the exposure of children to environmental chemicals, including the possibility that they may be more susceptible than adults to injury caused by those chemicals. The California Legislature passed the Children's Environmental Health Protection Act (Senate Bill 25, Escutia; Chapter 731, Statutes of 1999; "SB 25") to help address these concerns. Under SB25, OEHHA is mandated to consider infants and children specifically, where data permit, in evaluating the health effects of Toxic Air Contaminants (TACs).

The development of cancer is one of the adverse health effects that may occur in children as a result of exposure to environmental chemicals. The document "Prioritization of Toxic Air Contaminants under the Children's Environmental Health Protection Act" (OEHHA, 2001a) noted that risks of cancer from exposures to carcinogens occurring from conception through puberty can be different than those from exposures occurring in adulthood. Exposure to a carcinogen early in life may result in a greater lifetime risk of cancer for several reasons:

1. Cancer is a multistage process and the occurrence of the first stages in childhood increases the chance that the entire process will be completed, and a cancer produced, within an individual's lifetime.
2. Tissues undergoing rapid growth and development may be especially vulnerable to carcinogenic agents. During periods of increased cell proliferation there is rapid turnover of DNA, and more opportunity for misrepair of damage (*e.g.*, DNA breaks, crosslinks, adducts) or alterations to result in permanent changes to the DNA (*e.g.*, mutations, altered DNA methylation) that may ultimately lead to cancer.
3. During early development, a greater proportion of the body's cells are relatively undifferentiated stem cells, and as such represent a large target population of somatic cells capable of passing along permanent changes to the DNA during future cell divisions.
4. There may be greater sensitivity to hormonal carcinogens early in life since the development of many organ systems is under hormonal control (*e.g.*, male and female reproductive systems, thyroid control of CNS development).
5. Other factors that may play a role in increased cancer risk from exposures during critical developmental periods include differences in immunological activity, intestinal absorption, biliary and kidney excretion, blood and fat distribution, and expression of enzyme systems that activate or detoxify carcinogens.

Data in humans and animals for a variety of carcinogens suggest that exposures to such carcinogens early in life may result in a greater lifetime risk of cancer compared to exposures later in life. Examples of this effect in humans are carcinogenicity due to ionizing radiation, diethylstilbestrol (DES), chemotherapeutic agents, and tobacco smoke.
Ionizing radiation exposure carries an increased risk of cancer when exposures occur early in life compared to adult exposures for a number of tumor types. Children exposed to ionizing radiation (diagnostic X-rays) *in utero* demonstrate a larger excess of leukemia cases than children exposed to ionizing radiation postnatally (NRC, 1990). Exposure to radioisotopes (^{131}I, ^{137}Cs, ^{134}Cs, ^{90}Sr) as a consequence of the 1986 Chernobyl nuclear accident resulted in an elevated thyroid cancer

incidence in children but not adults (Moysich, 2002). Treatment of children for Hodgkin's lymphoma with both chemotherapeutic agents and irradiation has been shown to increase the risk of secondary tumors (Swerdlow et al., 2000; Franklin et al., 2006). Age at irradiation in Hodgkin's disease patients treated with radiotherapy strongly influenced the risk of developing breast cancer. The relative risk (RR) of developing breast cancer was 136 for women treated before 15 years of age, 19 for women 15-24 years of age, and 7 for those 24-29 years of age. In women above 30 years of age, the risk was not increased (Hancock *et al*., 1993).

DES was administered to pregnant women in the 1940s-1960s for the purpose of preventing pregnancy loss. In 1970, Herbst and Scully described 7 cases of vaginal adenocarcinoma (6 cases of the clear-cell type) in women aged 15-22 years. This type of cancer is extremely rare in that age range. A follow-up epidemiological study included an additional case, and noted the fact that the mothers of 7 of the 8 patients had been treated with DES during their pregnancy (Herbst *et al*., 1971). Reports by other investigators confirmed the association between maternal use of DES during pregnancy and the development of vaginal adenocarcinoma in their female offspring (Preston-Martin, 1989). It was observed that *in utero* DES exposure resulted in female genital tract morphological changes which correlated with both dose and duration of exposure, and those changes were not related to the maternal conditions which were the reason for the DES administration. Additionally, the risk of occurrence of those morphological changes declined with increasing gestational age at first exposure (O'Brien *et al*., 1979; Preston-Martin, 1989). In contrast, vaginal adenocarcinoma incidence did not increase in the exposed mothers themselves, indicating an increased early-life susceptibility to the carcinogenic effects of DES.

There is evidence in the epidemiological literature indicating that exposure to tobacco smoke during puberty may increase risk of breast cancer later in life, particularly among women who are NAT2 slow deacetylators (Marcus *et al*., 2000; Morabia *et al*., 2000; Lash and Aschengrau, 1999). Wiencke *et al*. (1999) report that early age at initiation of smoking is associated with a higher level of DNA adducts in lung tissue of former-smokers with lung cancer.

It has also been observed by Smith *et al*. (2006) that human *in utero* or early childhood exposure to arsenic in drinking water results in significantly increased lung cancer incidences during adult life.

Data from animal studies provide additional examples of increased sensitivity to early life (typically postnatal and juvenile) exposures. These effects span a range of target tissues, including the liver (vinyl chloride, safrole), brain (methylnitrosourea), reproductive tract (DES, tamoxifen), and lung (urethane) (OEHHA, 2001a).

In the following sections we summarize two efforts to evaluate quantitatively the effect of lifestage at exposure on carcinogenic response in experimental animal studies. The first section provides a description of OEHHA's analysis of data on the effect of age at exposure on carcinogenic potency. (Details of this analysis are in Appendix J.) The second section describes U.S. EPA's work in this area. (We also provide the published paper in Appendix I that presents the U.S. EPA analyses.) Both analyses used extant data available in the published literature. U.S. EPA used their analysis to modify the procedures they have used to estimate cancer risk by weighting risk by specific factors for childhood exposures. The weighting factors are a policy choice supported by U.S. EPA's data analysis. The results of OEHHA's analysis, summarized below and described in detail

in Appendix J, support the decision to modify policy to weight risk when exposure occurs during childhood.

OEHHA Analysis of the Effect of Age at Exposure on Cancer Potency

The analysis of animal cancer studies which include early life exposure by the Reproductive and Cancer Hazard Assessment Branch (RCHAB) of OEHHA also supports the application of lifestage-specific cancer potency factor adjustments. This analysis is provided in detail as Appendix J of this document.

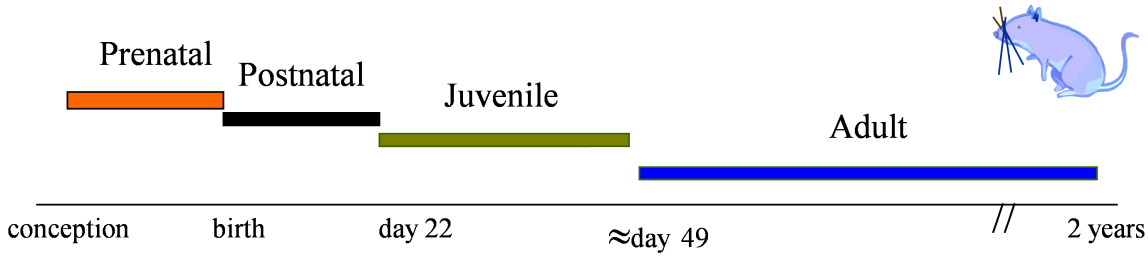
Early-in-life susceptibility to carcinogens has long been recognized by the scientific community and clinicians as a public health concern. Numerous scientific publications and symposia have addressed this issue over the years and the scientific literature contains a number of human clinical findings and epidemiological studies of early life cancer susceptibility. While there are many indications of increased human cancer susceptibility in early life, the magnitude of the impact has been difficult to gauge. Until recently risk assessment procedures have not in general addressed the issue. As described in the next section, in 2005 the U.S. EPA adopted an approach to weight carcinogens by age at exposure if they act via a mutagenic mode of action. The California legislature in 2000 directed OEHHA to assess methodologies used in addressing early-in-life risk, compile animal data to evaluate those methods, and develop methods to adequately address carcinogenic exposures to the fetus, infants, and children (Children's Environmental Health Initiative [AB 2872, Shelly]; California Health and Safety Code [HSC] section 901 [a] through [e]).

OEHHA assessed cancer risk assessment methodologies, and found that the existing risk assessment approaches did not adequately address the possibility that risk from early-in-life and adult exposures may differ. OEHHA further concluded that there was a need to address early-in-life cancer risk, and undertook studies to develop methods for doing so. Age-related cancer susceptibility data were identified from published animal cancer bioassays in which these issues were addressed. Two types of studies with early-in-life exposures were compiled. The first type are "multi-lifestage exposure studies." These studies have at least two groups exposed during different lifestages: One dose group is exposed to a chemical only during one of the following lifestages (Figure 3):

- prenatal (from conception to birth),
- postnatal (from birth to weaning),
- juvenile (from weaning to sexual maturity).

The second dose group is exposed for some period of time at an older age, preferably during the adult lifestage, that is, after sexual maturity. This group served as the reference group. In some cases where there was no adult exposure group, animals exposed as juveniles served as the reference group. Multi-lifestage exposure studies are available for many chemicals, enabling the exploration of patterns in early-life susceptibility across chemicals.

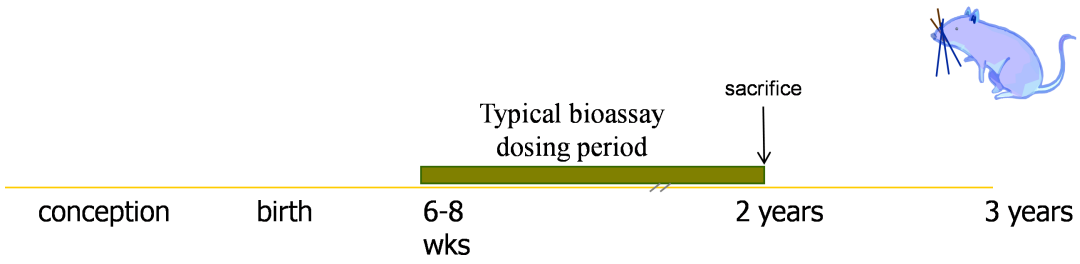
Figure 3. Definition of Rodent Lifestage Adopted in the OEHHA Analyses



OEHHA also conducted "chemical-specific case studies" of early-life sensitivity for two carcinogens, ethyl-N-nitrosoamine (DEN) and N-ethyl-N-nitrosourea (ENU) that combine data from a number of studies. These "chemical-specific case studies" were conducted to explore the feasibility of analyzing chemical-specific data on age susceptibility from single-lifestage exposure experiments. For these chemicals, OEHHA compiled from the literature a second type of study, "single-lifestage exposure experiments." In these experiments dose groups were exposed only during a particular lifestage and, unlike the "multi-lifestage exposure studies," there was no requirement that the same study also include groups exposed during a different lifestage. Thus, single-lifestage exposure experiments were identified as being either prenatal, postnatal, juvenile, or adult exposure studies. For each of the two chemicals, there were many prenatal studies conducted that were compiled, analyzed, and grouped together. Postnatal studies from different publications were similarly compiled, analyzed and grouped together, as were juvenile studies. Adult studies were not available for either DEN or ENU, thus for both chemicals juvenile exposure studies served as the referent for prenatal studies, and for postnatal studies.

Typical cancer bioassays such as those conducted in rats and mice by NTP involve exposing animals starting at six to eight weeks of age, which is the time at which these animals reach sexual maturity (late teenagers relative to humans). The experiments are run for two years, ending when the animal is in late middle age. Thus, early and very late life exposures are not included in the typical rodent bioassay (see Figure 4). If the NTP bioassay is used as a basis for estimating cancer potency, the potency and resulting risk estimates may be too low. Thus OEHHA focused on finding studies that evaluated early in life exposures.

Figure 4. Dosing Period for Typical Rodent Bioassays.



Since bioassays examining the effect of age at exposure on carcinogenesis were conducted by various investigators for different purposes, there is a great deal of variation across studies in terms of dose selection, duration of exposure, number of animals, and length of study duration. To be included in the compilation of studies with early life exposure, a study or an experimental group in a study had to meet minimum requirements.

The criteria for study inclusion are as follows:

- Treated groups were exposed to a single chemical carcinogen or a single carcinogenic chemical mixture.
- Study groups were not compromised by severe treatment-related non-cancer toxicity.
- Overall the duration of exposure period plus observation period exceeded 40 weeks, unless animals died of tumor.
- For included dose groups, the study must report age at dosing, age at sacrifice, and site-specific tumor incidence.
- Each lifestage exposure treatment group has an appropriate concurrent control group, or, for rare tumors only, an appropriate historical control.
- The studies were on mammals.
- Each treatment and control group consists of at least ten animals, unless the conduct and design of the study was well done in all other aspects (*e.g.*, the length of the study was sufficiently long to observe treatment-related tumors) and tumor incidence was high in treated groups and very low in controls.
- Site specific tumor data were reported, not only total number of tumor bearing animals.
- The test compound was administered in the diet, water, via gavage, or by intraperitoneal (i.p.), intravenous (i.v.), or subcutaneous (s.c.) injection. For dermal and subcutaneous injection studies, distal tumor findings are utilized (for dermal, other than skin tumors; for injection, non-injection site tumors).

- While studies designed to histopathologically examine tumors at multiple sites were preferred, studies that examined only a select set of organ/tissue sites were not excluded if the sites examined were known with confidence to be the only target tissues for the chemical and lifestage in question in that particular strain of animal.

Different approaches were taken to identify animal cancer studies that included groups of animals exposed during early life stages. First, MEDLINE and TOXLINE (National Library of Medicine) databases were searched using combinations of various key words for cancer (*e.g.*, tumor(s), neoplasm(s), cancer, neoplasia, cancerous, neoplasms-chemically induced) and for early-life exposure (*e.g.*, age, age-at-exposure, development (al), prenatal, *in utero*, gestation (al), postnatal, neonatal, juvenile, weaning, weanling, adolescent, adolescence, young). Second, the extensive compilation of bioassays in the *Survey of Compounds which have been Tested for Carcinogenic Activity*, was reviewed. This survey, formerly maintained by the National Cancer Institute as Public Health Service Publication Number 149, or PHS 149, is now available from a private source electronically as CancerChem, 2000. Third, from bibliographies from relevant published papers additional studies were identified. Finally the Single Dose Database developed by Calabrese and Blain (1999) was obtained and utilized to identify additional publications that appeared to contain potentially useful data. All of these publications were evaluated to determine if the study dosed separate groups of animals early in life and at or near adulthood. A total of 145 publications, providing data on 84 chemicals, were identified as meeting the criteria for study inclusion. A subset of these met the criteria for inclusion in the multi-lifestage exposure analysis.

Finally, for the OEHHA multi-lifestage analyses, we define "experiment" as a study component consisting of a control group as well as a treated group(s) exposed during the same lifestage (*i.e.*, prenatal, postnatal, juvenile or adult), and using the same experimental protocol (*e.g.*, route of exposure, strain, species, laboratory). Thus, by our definition one publication may report multiple experiments.

In the OEHHA analysis, data from studies on 23 unique carcinogens, 20 of which are considered to act via primarily genotoxic modes of action, were analyzed. Of these 20 carcinogens, 15 are thought to require metabolic activation to the ultimate carcinogenic species (Table 1). Fourteen carcinogens, including one thought to act via primarily nongenotoxic modes of action, were included in the prenatal multi-lifestage exposure studies. Eighteen carcinogens, including two thought to act via primarily nongenotoxic modes of action, were included in the postnatal multi-lifestage exposure studies. Five carcinogens were included in the juvenile multi-lifestage exposure studies. The case study chemicals, DEN and ENU, are both genotoxic. ENU is a direct acting alkylating agent, while DEN requires metabolic activation.

Table 1. Carcinogens for which studies with multi-lifestage exposures in animal studies are available

Genotoxic carcinogens requiring metabolic activation

Benzidine
Benzo[a]pyrene
Dibutylnitrosamine
Diethylnitrosamine (DEN)
7,12-Dimethylbenz[a]anthracene (DMBA)
Dimethylnitrosamine (DMN)
Di-n-propylnitrosamine (DPN)
1 -Ethyl-nitrosobiuret
2-Hydroxypropylnitrosamine
3-Hydroxyxanthine
3-Methylcholanthrene (3-MC)
4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)
Safrole
Urethane
Vinyl chloride

Genotoxic carcinogens not requiring metabolic activation

Butylnitrosourea
1,2-Dimethylhydrazine
Ethylnitrosourea (ENU)
Methylnitrosourea (MNU)
ß-Propiolactone

Nongenotoxic carcinogens

1,1-Bis(p-chlorophenol)-2,2,2-trichloroethane (DDT)
Diethylstilbestrol (DES)
2,3,7,8-Tetrachlorodibenzodioxin (TCDD)

Cancer Potency Estimation

Statistical methods were developed and used to analyze the data and derive measures of early-life susceptibility. These are described in detail in Appendix J. In brief, a cancer potency (the slope of the dose response curve) was developed for each of the experiments selected using the linearized multistage model. This model was chosen because of widespread use in risk assessment, and its flexibility in being able to fit many different data sets needed to evaluate the effect of lifestage-at-exposure on cancer potency. The dose metric used for the potency analyses is cumulative dose normalized to body weight. The cancer potency is thus expressed as the increase in tumor probability with increasing cumulative dose in units of mg/kg body weight.

To take into account uncertainty in potency estimation, cancer potencies are depicted by a statistical distribution, rather than by a single, fixed value, using methods described in Appendix J. While these methods have typically been used to obtain and report the 95th percentile of the cancer slope parameter for cancer risk assessment purposes, here OEHHA utilized the full distribution of the cancer slope parameter to derive measures of early-life susceptibility to carcinogens. This was done to systematically take into account uncertainty in the analysis.

For experiments where treatment related tumors were observed at multiple sites or at the same site but arising from different cell types, slopes from these sites were statistically combined by summing across the potency distributions (assuming independence across the sites that were observed) to create an overall multisite cancer potency. It is not uncommon that a carcinogen causes more than one type of cancer or causes tumors at different sites depending on lifestage at exposure. For example, in humans tobacco smoke causes cancers of the lung, bladder, and certain other organs. This multi-site carcinogenicity is frequently observed in animal experiments as well. In order to account for this, all treatment-related tumors that were observed in a given lifestage were taken into account in estimating cancer potency from that particular experiment.

Addressing Early-Age Sensitivity in Estimating Cancer Risk: Age Sensitivity Factors

Inherent Sensitivity of Lifestages – Lifestage Potency Ratios

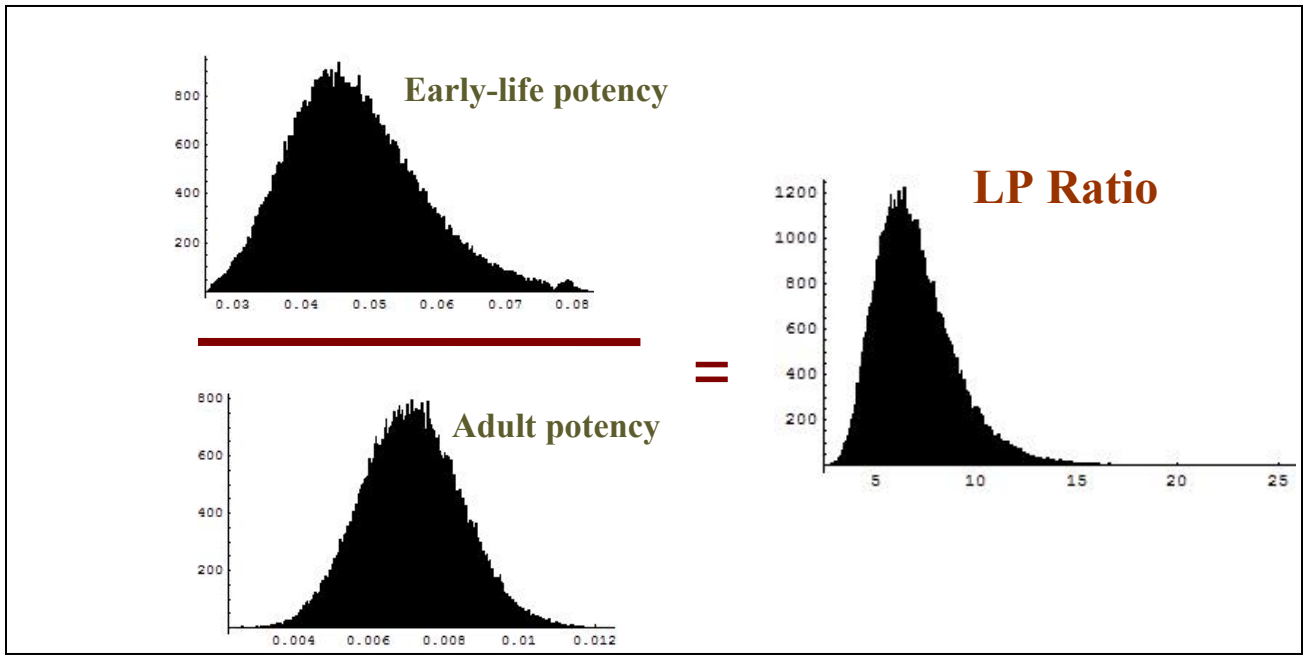
For this analysis, OEHHA calculates the ratio of cancer potency derived from an early lifestage exposure experiment(s) to that derived from an experiment(s) conducted in adult animals. OEHHA used the potency distributions for the individual lifestage exposures, rather than a point estimate, to derive the ratios. The lifestage cancer potency ratio is then described as a distribution and one can select specific percentiles from the distribution to better understand and bound the uncertainty (Figure 5). Of particular importance is the location of the ratio distribution in relation to the reference value of 1.0, which would mean no difference in risk from exposures at early versus adult lifestages. A lifestage cancer potency ratio distribution that primarily lies above the value of 1.0 indicates early life exposures to a carcinogen result in a stronger tumor response relative to adult exposure. Conversely, a lifestage cancer potency ratio distribution that mainly lies below the value of 1.0 indicates early life exposure to a carcinogen results in a weaker tumor response relative to adult exposure.

A lifestage potency (LP) ratio distribution was derived for each multi-lifestage study, resulting in 22 prenatal ratio distributions representing 14 unique carcinogens, 55 postnatal LP ratio distributions representing 18 unique carcinogens, and seven juvenile LP ratio distributions representing five unique carcinogens. The LP ratio distributions for a given early lifestage were combined into a single "LP ratio mixture distribution," in order to show the range of susceptibilities of that lifestage to the carcinogens studied.

LP ratio mixture distributions for a given early lifestage were developed by (1) obtaining a single LP ratio distribution for each chemical (when a chemical is represented by more than one study) and then (2) equally sampling across all chemicals. When a chemical is represented by more than one study, then the LP ratio distributions from all studies of that chemical were combined by equally sampling from each LP ratio distribution via Monte Carlo methods to obtain a single LP ratio distribution for that chemical. (Appendix J describes this in more detail, as well as a

sensitivity analysis that included two alternative sampling methods.) Once each chemical is represented by a single LP ratio distribution, then the LP ratio mixture distribution for each early lifestage (prenatal, postnatal, and juvenile) is obtained by equally sampling across all of the chemicals via Monte Carlo methods.

Figure 5. Lifestage Potency Ratio (LPR) distribution.

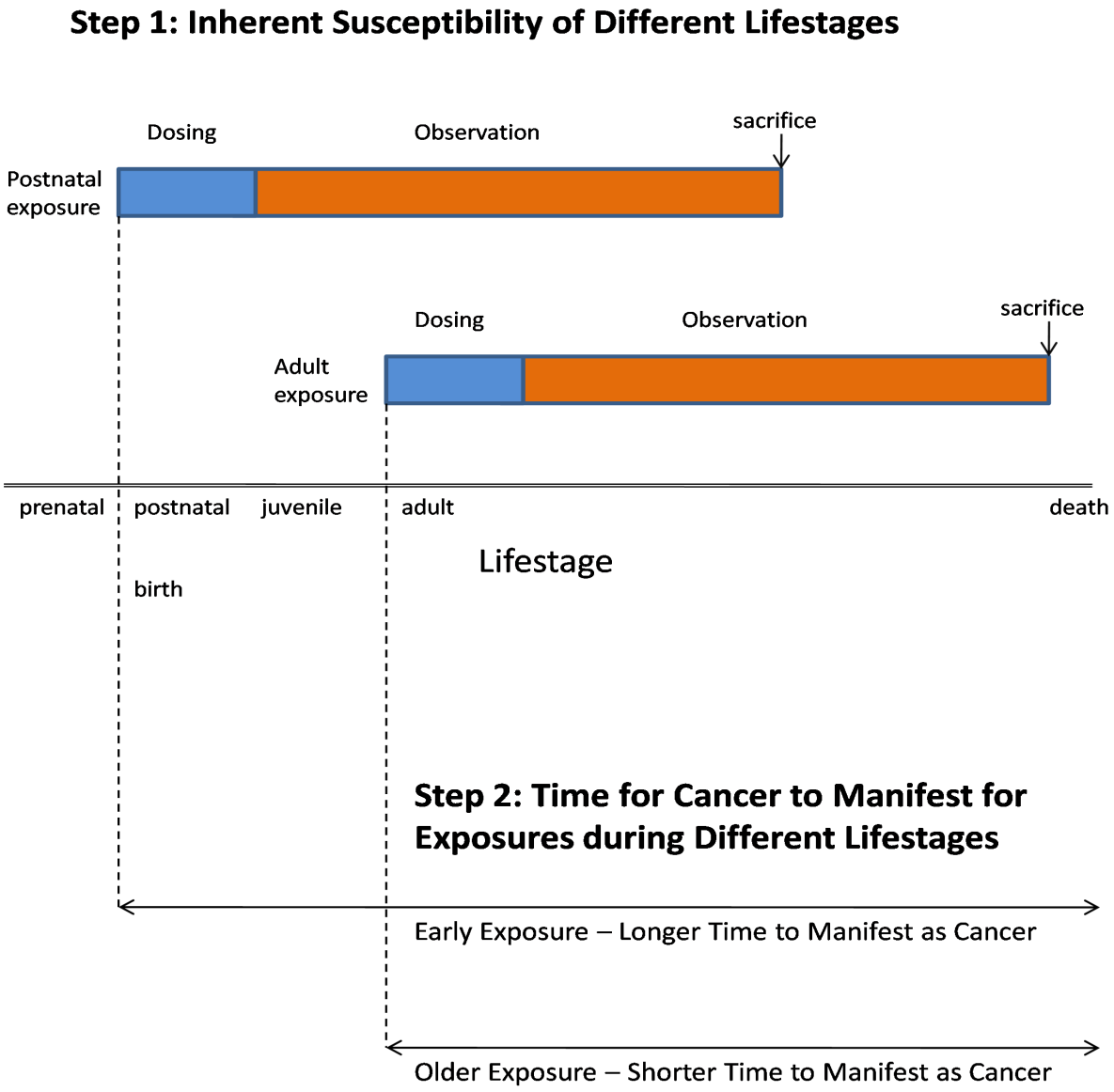


Effect of Longer Time Period for Cancer to Manifest

The LP ratios described above characterize the inherent susceptibility of early lifestages to carcinogen exposure, by comparing potencies for individuals followed for similar periods of time and similarly exposed, but exposed during different lifestages. Age-specific adjustments to the cancer potency must also take into account the longer period of time that carcinogen exposure to the young has to manifest as cancer. Empirical data from studies of both humans and animals demonstrate that, for many cancers, cancer risk increases with age, or time since first exposure. While some cancers have been seen to increase by as much as the sixth power of age, a general approach taken for example by the National Toxicology Program in analyzing tumor incidences in its chronic bioassays is to assume that cancer risk increases by the third power of age. Thus, consistent with the approach used by the NTP in analyzing rodent cancer bioassay data, the longer period of time that exposed young have to develop tumors is addressed by taking into account time-of-dosing. This was done by multiplying the LP ratio by a time-of-dosing factor, to yield an age sensitivity factor (ASF). Specifically, the prenatal LP ratio is multiplied by a factor of 3.0, the postnatal LP ratio is multiplied by a factor of 2.9, and the juvenile LP ratio is multiplied by 2.7. Thus, ASFs were developed for each experiment, by first calculating the LP ratio to address inherent susceptibility of early lifestages relative to adults, and then accounting for the effect of years available to manifest a tumor following carcinogen exposure. (see Figure 6). Note that we

are not using the term "sensitivity" in the immunologic sense (*e.g.*, sensitization), but rather are using the term more generically.

Figure 6. Issues addressed by the Age-Sensitivity Factor (ASF)



Application of this approach for risk associated with lifetime exposures would include an ASF of less than 1 for exposures during the latter part of adult life for carcinogens that act on early stages. Therefore, the addition of this adjustment to the younger lifestages but not to the later part of the adult period could overestimate the risk of whole-life exposures. On the other hand, the 70 year "lifetime" used in estimating lifetime cancer risk does not reflect the longer lifespan of the U.S. population. Further, as noted above, the animal bioassays on which potency was based typically exclude pre-weaning dosing and sacrifice animals during their late middle-age. Use of cancer potencies calculated from standard assays can therefore underestimate lifetime cancer risk. The ASF calculated for carcinogens includes both inherent sensitivity of developing animals and the available time since exposure to develop cancer.

Results of OEHHA Analysis

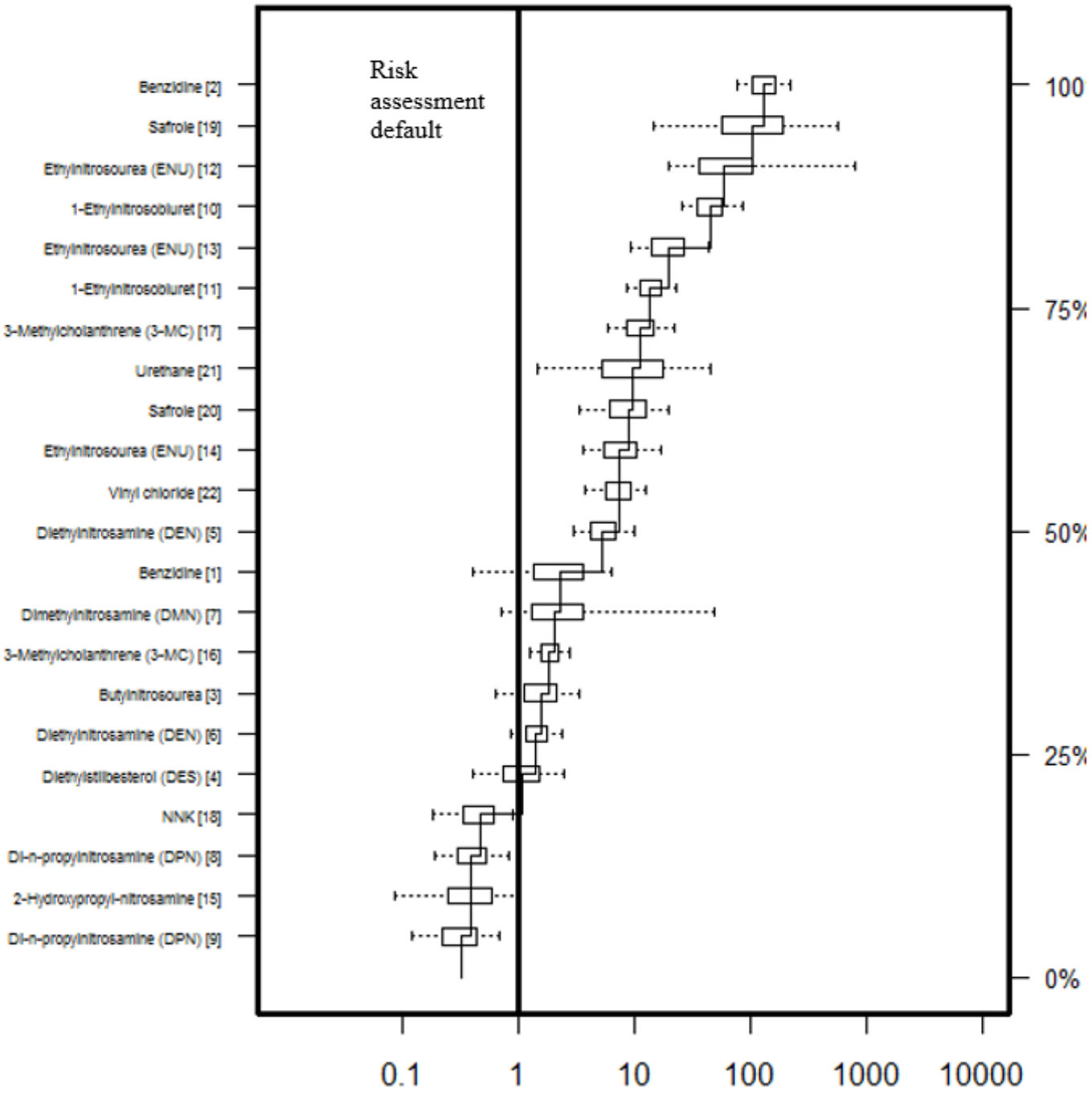
The analyses indicate that both the prenatal and postnatal lifestages can be, but are not always, much more susceptible to developing cancer than the adult lifestage. The analyses also indicated that the ASFs for these age windows vary by chemical, gender and species.

Regarding prenatal lifestage exposure, few cases were indicative of equal inherent adult and prenatal susceptibility, with an LP ratio of unity. The LP ratio distribution was roughly bimodal, with LP ratios for several studies significantly greater than unity and several others significantly less than unity. Figure 7 below shows the ASFs from each of the prenatal multi-lifestage exposure studies, displayed as a cumulative frequency profile. The median of the prenatal ASF mixture distribution was 2.9 (see also Table 6 in Appendix J),

The modality in the prenatal LP ratio distribution was reflected in the DEN and ENU case studies, with results for DEN suggesting inherently less sensitivity than older animals from exposure *in utero*, and for ENU just the opposite. For the DEN and ENU case studies, the referent groups were juvenile rather than adult animals, and the results may have underestimated the LP ratio and ASF, to the extent that some of the apparent sensitivity for DEN and ENU in the prenatal period carries through to the juvenile period. ENU is a direct acting carcinogen that does not require metabolic activation, whereas DEN can not be metabolized to any significant extent by fetal tissues until relatively late in gestation. This may explain the lower fetal susceptibility of DEN. However, prenatal metabolic status is not the sole determinant of prenatal susceptibility; *e.g.*, benzidine and safrole require metabolic activation and exhibit greater susceptibility from prenatal exposure.

The median of the postnatal ASF mixture distribution was 13.5 (see Table 7 in Appendix J). Figure 8 below shows the ASFs from each of the postnatal multi-lifestage exposure studies, displayed as a cumulative frequency profile. Thus, for the chemicals studied, there was generally greater susceptibility to carcinogens during the early postnatal compared to the adult period, particularly when the ASF accounts for the longer period cancer has to manifest when exposure occurs early in life. The DEN and ENU case studies also exhibited substantial extra susceptibility during the postnatal period. To summarize, for most of the carcinogens studied here, rodents are inherently more sensitive in the postnatal period, as indicated by Figure 8.

Figure 7. Prenatal ASF Cumulative Frequency Profile

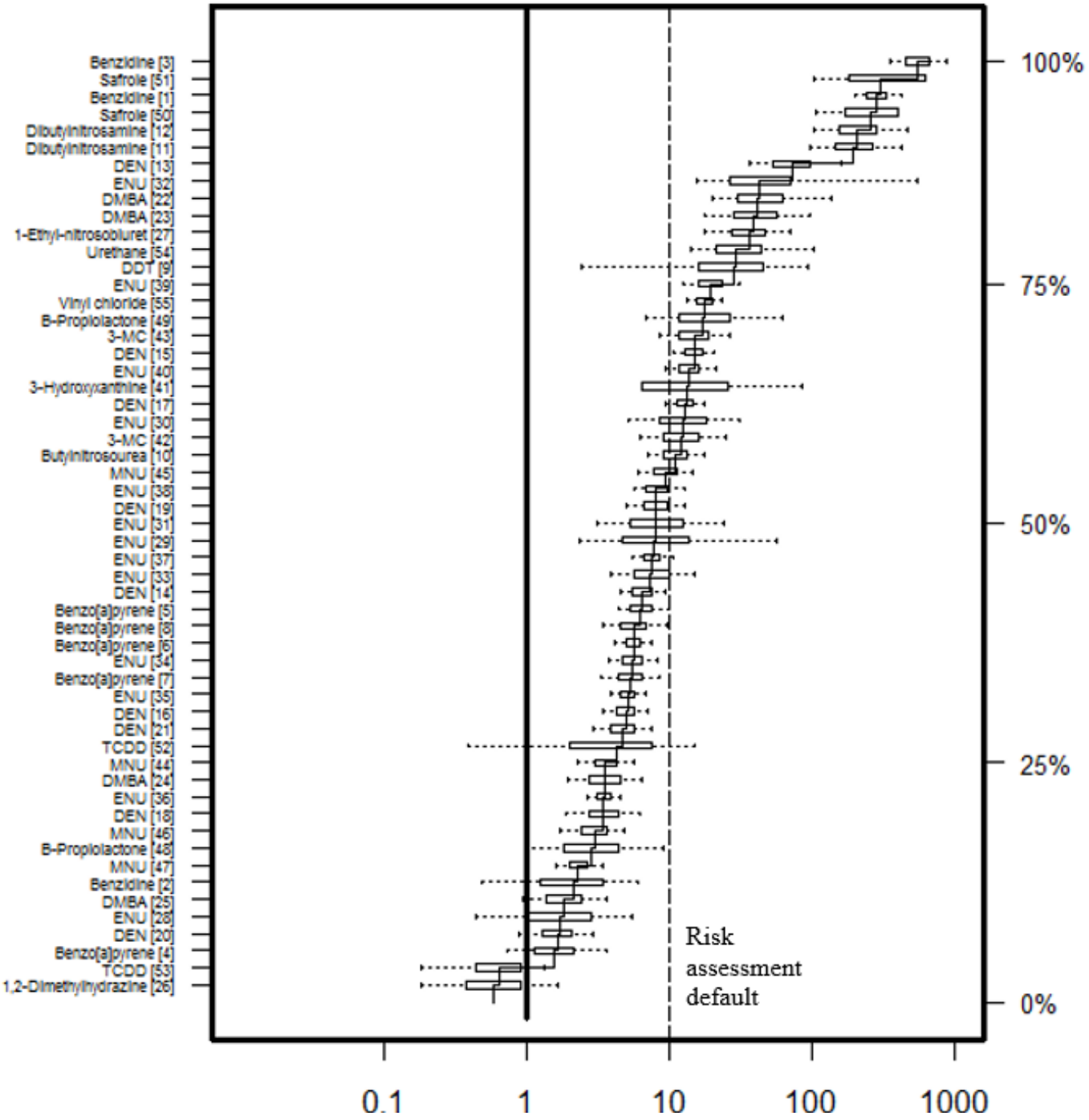


The median of the prenatal ASF mixture distribution was 2.9 (see also Table 6 in Appendix J). References are given in the legend on the next page

Figure 7 Legend (References as in Appendix J)

1. Vesselinovitch *et al*. (1979a), mouse, B6C3F$_1$, F, day -9 to 0
2. Ibid, M, day -9 to 0
3. Zeller *et al*. (1978), rat, Sprague Dawley, M/F day -2
4. Turusov *et al.* (1992), mouse, CBA, F, day -2
5. Mohr et al. (1975), hamster, Syrian Golden, day -15 to -1
6. Mohr *et al*. (1995), hamster, Syrian Golden, F, day -3
7. Althoff *et al*. (1977), hamster, Syrian Golden, M/F, day -9 to -3
8. Ibid, day -9 to -3
9. Althoff and Grandjean (1979), hamster, Syrian Golden, F, day -9 to -3
10. Druckrey and Landschutz (1971), rat, BD IX, M/F, day -10
11. Ibid, day -3
12. Naito *et al*. (1981), rat, Wistar, day -9
13. Ibid, day -9
14. Tomatis *et al*. (1977), rat, BDVi, F, day -5
15. Althoff and Grandjean (1979), hamster, Syrian Golden, M/F, day -9 to -3
16. Tomatis *et al*. (1971), mouse, CF-1, F day -4 to -1
17. Turusov *et a*l. (1973), mouse, CF-1, F, day -2
18. Anderson *et al.* (1989), mouse, C3H & B6C3 F$_1$,M/F day -8 to -4
19. Vesselnovitch *et al.* (1979a), mouse, B6C3 F$_1$, M, day -9 to -3
20. Vesselnovitch *et al.* (1979b), mouse, B6C3 F$_1$, F day -9 to -3
21. Choudari Kommineni *et al*. (1970), rat, MRC, M/F, day -4
22. Maltoni *et al.* (1981), rat, Sprague Dawley, M/F day -13 to -7

Figure 8. Postnatal ASF Cumulative Frequency Profile



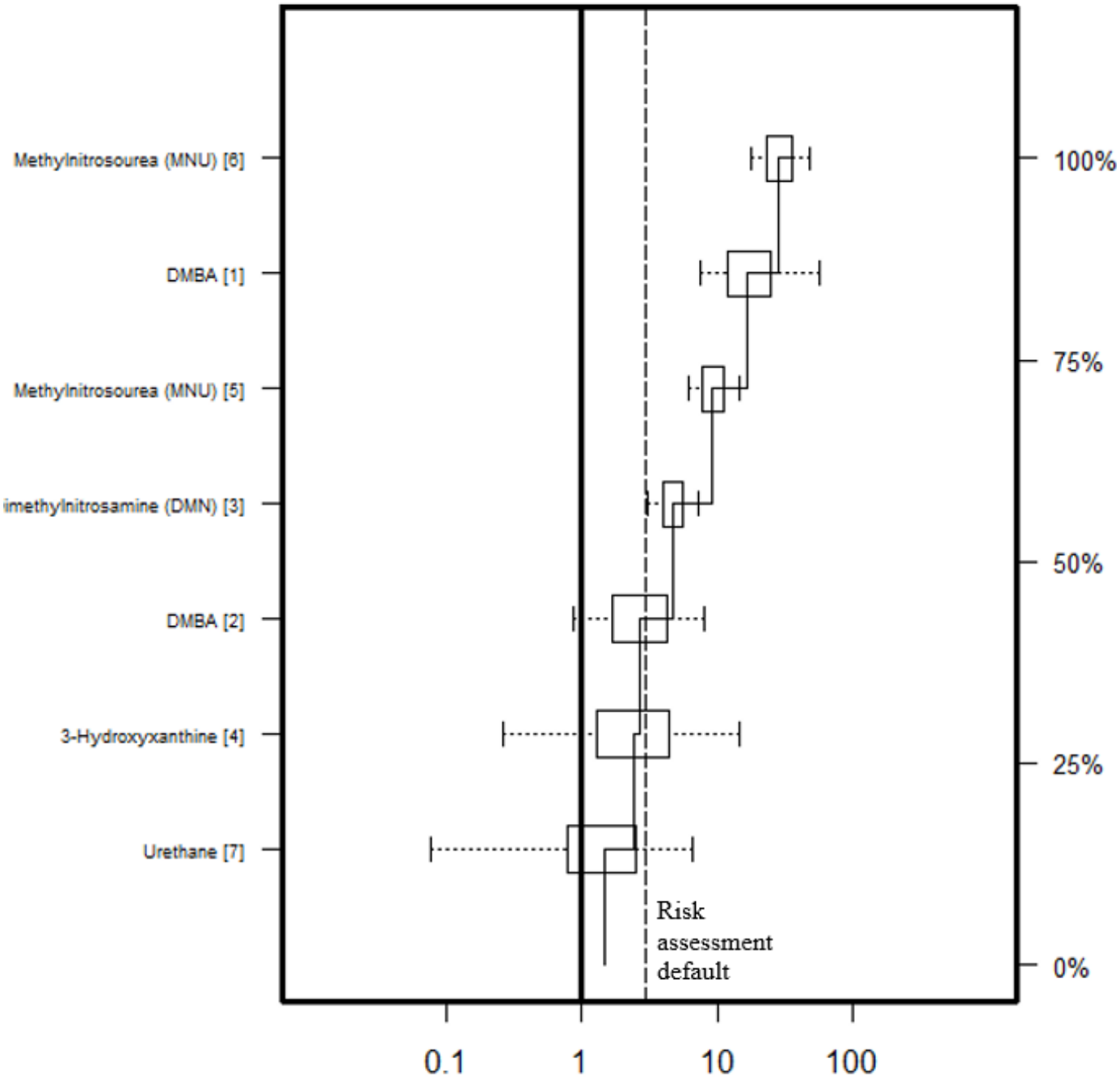
The median of the postnatal ASF mixture distribution is 13.5. The dotted line represents the default ASF for weighting risk for carcinogen exposures to humans between the third trimester and 2 years of age (see next section). References are given in the legend on the next page.

Figure 8 Legend (References as in Appendix J)

1 Vesselinovitch *et al.* (1975b), mouse, B6C3F$_1$, M, day 7-27
2 Vesselinovitch *et al.* (1979), mouse, B6C3F$_1$, F, day 1-21
3 Ibid, M, day 1-21
4 Truhaut *et al.* (1966), mouse, swiss, M/F, day 1
5 Vesselinovitch *et al.* (1975a), mouse, B6C3F$_1$, F, day 1
6 Ibid, M, day 1
7 Ibid, C3A F$_1$, F, day 1
8 Ibid, M, day 1
9 Vesselinovitch *et al.* (1979a), mouse, B6C3F$_1$, M, day 1-28
10 Zeller *et al.* (1978), rat, Sprague Dawley, M/F, day 2
11 Wood *et al.* (1970), mouse, IF x C57, F, day 1-15
12 Ibid, M, day 1-15
13 Rao and Vesselinovitch (1973), mouse, B6C3F$_1$, M, day 15
14 Vesselinovitch *et al.* (1984), mouse, B6C3F$_1$, F, day 1
15 Ibid, M, day 1
16 Ibid, F, day 15
17 Ibid, M, day 15
18 Ibid, C3A F$_1$, F, day 1
19 Ibid, M, day 1
20 Ibid, F, day 15
21 Ibid, M, day 15
22 Meranze *et al.* (1969), rat, Fels-Wistar, F, day 10
23 Ibid, M, day 10
24 Walters (1966), mouse, BALB/c, F, day 17
25 Ibid, M, day 17
26 Martin *et al.* (1974), rat, BDIX, M/F, day 10
27 Druckrey and Landschutz (1971), rat, BDIX, M/F, day 10
28 Naito *et al.* (1985), gerbil, mongolian, F, day 1
29 Ibid, M, day 1
30 Bosch (1977), rat, WAG, F, day 8
31 Ibid, M, day 8
32 Naito *et al.* (1981), rat, Wistar, F, day 7
33 Ibid, M, day 7
34 Vesselinovitch *et al.* (1974), mouse, B6C3F$_1$, F, day 1
35 Ibid, M, day 1
36 Ibid, F, day 15
37 Ibid, M, day 15
38 Ibid, C3A F$_1$, F, day 1
39 Ibid, M, day 1
40 Ibid, M, day 15
41 Anderson *et al.* (1978), rat, Wistar, F, day 9
42 Klein (1959), mouse, A/He, F, day 8-31
43 Ibid, M, day 8-31
44 Terracini and Testa (1970), mouse, B6C3F$_1$, F, day 1
45 Ibid, M, day 1
46 Terracini *et al*. (1976), mouse, C3Hf/Dp, F, day 1
47 Ibid, M, day 1
48 Chernozemski and Warwick (1970), mouse, B6A F$_1$, F, day 9
49 Ibid, M, day 9
50 Vesselinovitch *et al*. (1979a), mouse, B6C3F$_1$, M, day 1-21
51 Vesselinovitch *et al*. (1979b), mouse, B6C3F$_1$, M, day 1-21
52 Della Porta *et al*. (1987), mouse, B6C3F$_1$, F, day 10-45
53 Ibid, M, day 10-45
54 Choudari Kommineni *et al*. (1970), rat, MRC, M/F, day 1-17
55 Maltoni *et al*. (1981), rat, Sprague Dawley, M/F, day 1-35

There were only five chemicals and seven studies, two of which were not independent, available to examine susceptibility in the juvenile period. The juvenile LP ratios indicated significantly greater susceptibility in this period for three independent studies, with the remaining studies consistent with equal inherent susceptibility to adult animals (see Figure 16 in Appendix J). Figure 9 below shows the ASFs from each of the juvenile multi-lifestage exposure studies, displayed as a cumulative frequency profile. The median of the juvenile ASF mixture distribution was 4.5 (see Table 8 in Appendix J).

Figure 9. Juvenile ASF Cumulative Frequency Profile



The median of the juvenile ASF mixture distribution is 4.5. The dotted line represents the default value for weighting risk for carcinogen exposures between 2 and 15 years of age (see next section).

Figure 9 Legend (References as in Appendix J)

1. Meranze *et al.* (1969), rat, Fels-Wistar, F, day 45
2. Ibid, M, day 45
3. Noronha and Goodall (1984), rat, CRL/CDF, M, day 46
4. Anderson *et al*. (1978), rat, Wistar, F, day 28
5. Grubbs *et al*. (1983), rat, Sprague Dawley, F, day 50-57; adult comparison group dosed on days 80-87
6. Ibid, F, day 50-57; adult comparison group dosed on days 140-147
7. Choudari Kommineni *et al*. (1970), rat, MRC, M/F, day 28-43

The studies that comprise the set of multi-lifestage exposure studies available for these analyses were not homogeneous. That is, they do not represent observations from the same distribution. Sensitivity analyses were conducted to test the robustness of the findings to different procedures for analyzing data and combining results. Of the methods used to combine the LC ratio distributions for underlying studies within each lifestage, the method of equally weighting studies within a chemical appeared to best represent the available data.

In calculating the ASF, to take into account the longer period of time for early carcinogen exposures to result in tumors, the hazard function was assumed to increase with the third power of age. This assumption is standard and has been borne out by a number of observations (Bailer and Portier, 1988). If the true rate of increase with age is greater than that, then the use of these ASFs may result in underestimates of the true sensitivity of these early life stages.

As the multi-lifestage exposure and case studies show, there appears to be considerable variability in age-at-exposure related susceptibility across carcinogens. There is also variability in age-at-exposure related susceptibility among studies of the same carcinogen. The sources of variability evident in the analyzed studies include timing of exposure within a given age window, and gender, strain, and species differences in tumor response. The set of studies identified and analyzed was not sufficiently robust to fully describe the variability quantitatively. This variability raises concerns that selection of the median (the 50^{th} percentile) estimates may considerably underestimate effects for certain agents or population groups. Relatively large variability in humans in response to carcinogens is expected to be common (Finkel, 1995). On the other hand, the numbers of carcinogens represented in the available data are limited and may not be representative of the population of carcinogens to which we are exposed (*e.g.*, greater than 500 on the Proposition 65 list alone). Thus, the size of the weighting factors used to weight risk by age at exposure is a policy decision.

Several of the carcinogens studied induced tumors at multiple sites in the same experiment, and at different sites, depending upon the lifestage during which exposure occurred. For these cases the combined multisite potency distribution referred to above was the basis for the lifestage comparison. This approach differs from other researchers investigating early vs. late in life differences who focused on tumor site-specific measures of carcinogenic activity (*e.g.*, Barton *et al*., 2005; Hattis *et al*., 2004, 2005). OEHHA believes that use of combined multisite potency distributions provides a more complete approach for considering age specific differences in carcinogenic activity. However, the observation that early life is generally a period of increased

susceptibility was similarly found using the tumor site-specific approach by these other researchers.

One limitation of the approach was the focus on lifestages, without attempting to describe changes in susceptibility that occur within a lifestage. Timing of carcinogen exposure within a given age window can affect the cancer outcome. For example, experiments with 1-ethyl-1-nitroso-biuret in prenatal and adult rats showed a three-fold difference in activity between groups exposed on prenatal day -10 versus prenatal day -3. In a second example, female rats exposed early in the adult period were more than three times as sensitive to the breast cancer effects of MNU as females exposed six weeks later. In general, the adult comparison groups in the multi-lifestage exposure studies were fairly young. The extent to which this may result in an overall bias of the results presented here is unclear. Also, for several cases, juvenile animals were used as the later life exposure group. In these cases the ASFs are likely underestimates of the relative sensitivity of the prenatal and postnatal lifestages, compared to that of the adult lifestage.

Excluded from the analysis were early in life studies in which the period of exposure for a specific exposure group crossed multiple lifestages. An example of results from studies of this type is provided by mouse studies for two non-genotoxic carcinogens, diphenylhydantoin (Chhabra *et al*., 1993a) and polybrominated biphenyls (PBBs) (Chhabra *et al*., 1993b), in which exposures began prior to conception, and continued throughout the prenatal, postnatal, and post-weaning period, up to the age of eight weeks. The data demonstrate an increased sensitivity of the early life period. Some studies that crossed multiple lifestages were included in the analyses of Barton *et al*. (2005) (Appendix I), which are consistent with the general conclusions discussed above.

Selection of Default Age-Sensitivity Factors (ASF)

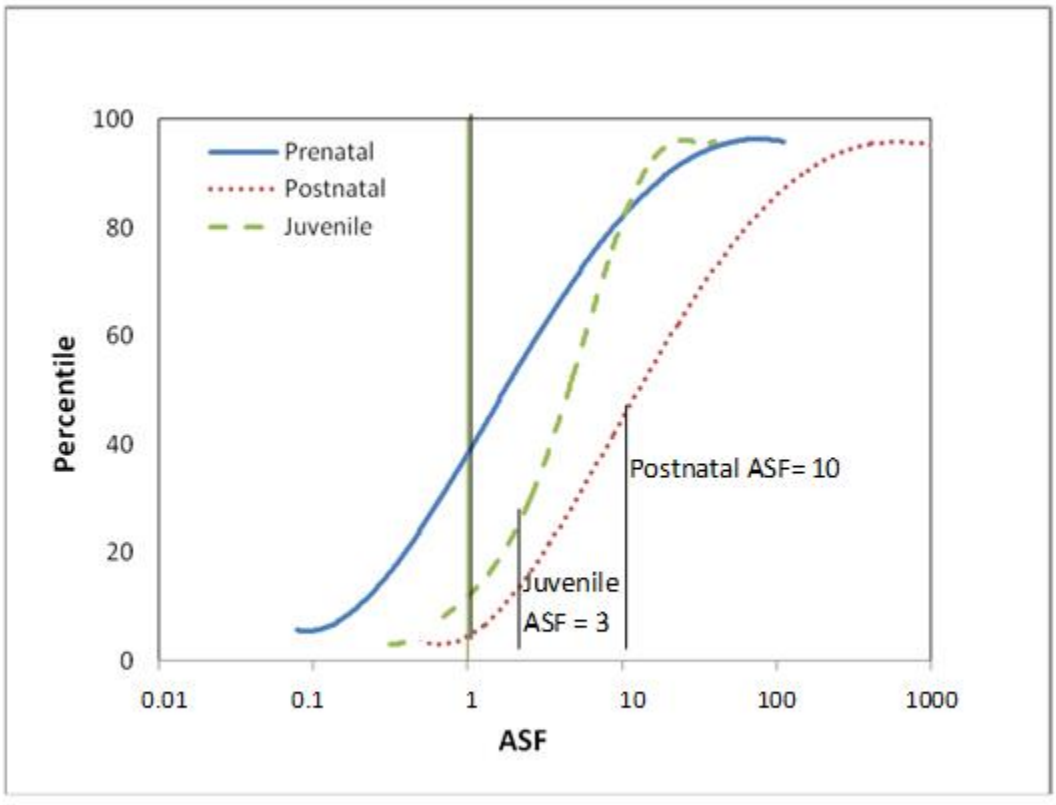
Selection of appropriate values to use to weight exposures that occur early in life using default ASFs for prenatal, postnatal and juvenile exposures is complicated by the limited database of chemicals and studies available for analysis, and the broad distribution of results for different chemicals as is shown in Figure 7, Figure 8, and Figure 9 (see also Appendix J). In view of the variability thus shown, and the considerable uncertainty in applying conclusions from this relatively small set of chemicals to the much larger number of chemicals of concern, it is probably unreasonable to specify a default ASF with greater than half-log precision (*i.e.* values of 1, 3, 10, 30 etc.). Further, rodents are born at a stage of maturity that approximates a third trimester human. Therefore, in the absence of chemical-specific data, OEHHA proposes to apply a default ASF of 10 for the third trimester to age 2 years, and a factor of 3 for ages 2 through 15 years to account for potential increased sensitivity to carcinogens during childhood. A factor of 10 falls just below the median estimate of the ASF for postnatal studies. This is also the value selected by U.S. EPA; while it is consistent with the OEHHA analysis, it may underestimate risk for some chemicals. The broad distribution of observed chemical-specific sensitivity ratios clearly indicates that there are some chemicals for which the sensitivity ratio is much larger than 10. Further research is needed to develop criteria for identifying these cases. Similarly, a factor of 3 for juvenile exposures is consistent with the range of estimates derived from the multi-lifestage exposure studies, and falls close to the median juvenile ASF estimate. It is acknowledged that there are few data available on which to base an estimate for the juvenile period. A factor of 3 adjusts for the longer time available for cancer to manifest, but may not fully account for some inherent differences in susceptibility to cancer, for example the observed susceptibility of breast tissue of

pubescent girls exposed to radiation. For specific carcinogens where data indicate enhanced sensitivity during lifestages other than the immediate postnatal and juvenile periods, or demonstrate ASFs different from the default ASFs, the chemical-specific data should be used in order to adequately protect public health.

The ASFs will be applied to all carcinogens, regardless of the theorized mode of action. While U.S. EPA currently intends to apply weighting factors only to those carcinogens with "a mutagenic mode of action" (U.S.EPA, 2005), OEHHA notes that there is evidence that early life is a susceptible time for carcinogens that are thought to act via non-mutagenic mode of action (DES is a prime example). Defining a mutagenic mode of action may be problematic if approached narrowly (ERG, 2008). Further, carcinogens may have multiple modes of action and one mode may predominate over other modes at different lifestages. The complexity of carcinogenesis argues against restricting the ASF to chemicals acting via a mutagenic mode of action.

Figure 10 provides a visual comparison of the ASF mixture distributions for the three early-life stages, prenatal, postnatal, and juvenile. In this figure, which is in log space, the policy choice of an ASF of 10 for exposures during the third trimester to age 2 years and 3 for the period of life from 2 to 15 years of age are indicated as vertical lines. It is apparent from this figure that weighting risk from exposures to carcinogens early in life is well-supported.

Figure 10. Prenatal, Postnatal, and Juvenile ASF Mixture Distributions and relation to default ASFs



OEHHA recognizes the limitations in the data and analyses presented, as discussed above. However, the analyses do provide some guidance on the extent to which risk may be over or underestimated by current approaches. While there is a great deal of variability across chemicals in the prenatal ASFs, the data indicate that the potency associated with prenatal carcinogen exposure is not zero. A factor of 3 is close to the median ASF, while a factor of 10 falls roughly at the 70th percentile of the prenatal ASF estimate. An ASF could be applied as a default when calculating lifetime cancer risk in humans arising from carcinogen exposures that occur *in utero*. In view of the considerable variability in the data for different carcinogens and the limited database available for analysis, OEHHA is not proposing the application of a specific factor to cancer potency estimates for prenatal exposures in the first and second trimesters as a default position in these Guidelines. However, given that the rodent is born at a stage of maturation similar to a third trimester fetus, it is reasonable to include the third trimester in the 10X potency weighting proposed up to age 2 years. The applicability of a cancer potency adjustment factor for first and second trimester prenatal exposure will be evaluated on a case-by-case basis, and may be used as evidence develops that supports such use. The consideration of prenatal exposures, including application of an appropriate susceptibility factor, would not make a large difference for risk estimates based on continuous lifetime exposures, due to the relatively short duration of gestation. However, risk estimates for short-term or intermittent exposures would be slightly increased by inclusion of the risks to the fetus during the prenatal period. Thus, risk may be underestimated when the first and second trimesters are excluded from the analysis.

Age Bins for Application of ASFs

The choice of human ages to which the ASFs apply is based on toxicodynamic and toxicokinetic considerations. Important toxicodynamic factors related to susceptibility to carcinogens include the rate of cellular proliferation and differentiation, which is quite high during organ maturation. In addition, toxicokinetic differences by age are important, due to impacts on detoxification and clearance of carcinogens (see following section). OEHHA's analysis of the influence of age-at-exposure on carcinogenesis broke the experimental rodent data into age bins that we termed "lifestages" including prenatal, "postnatal" (birth to weaning, about day 21) and "juvenile" (weaning to sexual maturation, or about day 22 to about day 49). Experiments were placed into the lifestage bins if exposure occurred at some time during the experimental rodent age bin.

There is no simple way to compare the rodent age groups used in the OEHHA analysis of available data to equivalent age groups in humans. Complicating factors include variations in organ system structural and functional maturation both within and between species. Further, the rodent age bins were chosen by gross indicators of development namely birth, weaning and sexual maturation, not on the basis of known susceptibility to carcinogenesis. Thus, critical factors relating to carcinogen susceptibility by age are the focus of the choice of human age bins to which the ASFs of 10 and 3 apply, rather than an attempt at exact correlation of rodent lifestage bin with human age.

The investigations used by OEHHA to evaluate the relationship between age at exposure and cancer potency were not conducted by standardized protocol. Further, the windows of susceptibility are quite varied by chemical and organ system, even within the lifestages defined in the OEHHA analysis. This complicates choosing a default ASF and the human age bin to which it applies. Examples from animal studies provided in Appendix J include the chemical diethylnitrosamine (DEN). The cancer potency varied over several orders of magnitude depending

on when during gestation and postnatal life the exposure occurred. A three-fold difference in potency between exposure on prenatal day -3 and prenatal day -10 is noted for 1-ethyl-1-nitrosobiuret in rats. There are also human examples of extensive variation of potency by age at exposure, including radiation, DES, and chemotherapeutic agents. The diversity of responses to different agents obviously underscores uncertainty in the choice of age bins to apply the default ASFs. However, the ASFs are a ***default*** to use when you have no chemical-specific data on influence of age-at-exposure on potency in order to protect public health. There will always be specific chemical examples where the ASF for either the third trimester-<2 yrs or 2-<16 yrs age bin is quite a bit larger or quite a bit smaller than the default.

In the following sections, we discuss our logic in proposing age bins of third trimester to age 2 years, and 2 to age <16 years to which the ASFs of 10 and 3 apply, respectively, and indicate the impact on risk estimates of these age bins.

Toxicokinetic Factors Relevant to Age Bins

Choice of the age-bins to which the default ASFs are applied is based on our understanding of the two primary drivers of age-related sensitivity to carcinogens, namely age-related toxicokinetic factors and toxicodynamic factors. In the case of toxicokinetics, the largest postnatal differences in xenobiotic metabolic capability occur between infants and adults. As noted in OEHHA (2001) and reviewed in detail elsewhere (*e.g.*, Cresteil et al., 1998; Ginsberg et al., 2004), hepatic drug metabolism by the cytochrome P-450 family of enzymes and the Phase II conjugating enzymes undergoes a maturation process during the first few years of life. The hepatic cytochrome P-450 enzymes exist in fetal isoforms at birth, and progressively change to adult isoforms at a relatively early stage of postnatal development. Thus, in humans the metabolic capability towards prototypical substrates develops over the first year of life towards adult levels. Similarly, the largest differences in metabolic capability of Phase II enzymes (conjugation of xenobiotic metabolites prior to excretion) tend to be between infants and adults. Other factors such as renal capability also are most different between neonates and adults. Thus, the first 2 years of life would encompass the increased sensitivity of early life stages due to toxicokinetic differences between early life and adulthood.

Ontogeny of Cytochrome P-450 Enzymes in Humans.

Cresteil (1998) describes three groups of neonatal cytochrome P-450: Cyp3A7 and Cyp4A1 present in fetal liver and active on endogenous substrates; an early neonatal group including Cyp2D6 and 2E1 which surge within hours of birth; and a later developing group, Cyp3A4, Cyp2Cs, and Cyp1A2. Total Cyp 3A protein, a major cytochrome P-450 enzyme responsible for biotransformation of many xenobiotics, is relatively constant in neonates and adults. However, Cyp3A7 is the primary fetal form (Hakkola et al., 1998), while Cyp3A4 is the primary adult hepatic form of the 3A series. At one month Cyp3A4 activity is about one-third of that in the adult liver (Lacroix et al., 1997; Hakkola et al., 1998). Allegaert *et al*. (2007) stated that Cyp3A4 (testosterone-6ß-hydroxylase) activity equaled or exceeded adult activity after 1 year of age. Cyp2E1, which metabolizes benzene, trichloroethylene and toluene, among others, increases gradually postnatally, reaching about one-third of adult levels by one year of age and attains adult levels by 10 years of age (Vieira et al., 1996; Cresteil, 1998). Cyp1A2, and Cyp2C9 and 2C19, the most abundant Cyp2 enzymes in adult human liver, appear in the weeks after birth, and reach

30% to 50% of adult levels at about 1 year of age (Treluyer et al., 1997; Hines and McCarver, 2002). Cyp1A1 is expressed in fetal liver where it can activate such xenobiotics as benzo[a]pyrene and aflatoxin B1 (Shimada et al., 1996), but is less important in adult liver (Hakkola et al., 1998).

Ontogeny of Cytochrome P-450 Enzymes in Rodents.

Hart et al. (2009) report developmental profiles of a number of cytochrome P-450 enzymes (measured as levels of mRNA transcripts of the specific genes) in mice. They identified three groups of isoforms. Group 1 (Cyp3A16 in both sexes; Cyp3A41b in males) appeared rapidly after birth but declined to essentially zero at 15-20 days, which is the period of weaning in mice. A second group (Cyp2E1, Cyp3A11 and Cyp4A10 in both sexes; Cyp3A41b in females) also increased rapidly after birth, but reached a stable maximal level by postnatal day 5. The third group (Cyp1A2, Cyp2A4, Cyp2B10, Cyp2C29, Cyp2D22, Cyp2F2, Cyp3A13 and Cyp3A25) were expressed only at low levels until days 10 to 15, but reached high stable levels by day 20.

ElBarbry et al. (2007) examined the developmental profiles of two toxicologically significant cytochrome P-450 enzymes, Cyp1A2 and Cyp2E1 in rats. mRNA transcripts of these genes were very low postnatally, but thereafter increased to reach a peak at or shortly after weaning (postnatal day 21 - 28 for rats). Immunoreactive Cyp1A2 and Cyp2E1 proteins were first detectable at postnatal day 3 and reached 50% of adult levels at weaning and adult levels at puberty. Differences in profiles between gene expression as mRNA and appearance of specific proteins as determined by immunoassay may reflect changes in the relative importance of transcription and translation control processes at various phases in development. Enzyme activities characteristic of Cyp1A2 and Cyp2E1 were found to parallel gene expression levels (ElBarbry et al., 2007) rather than immunodetectable protein levels, so there may also be issues of cross-reactivity between these two isoenzymes and others for which gene expression was not measured in these experiments.

In summary, the gene expression data in rats and mice show differences in details, but broadly resemble one another in that the main changes occur in the early postnatal period, with the major adjustments completed at or around the time of weaning, although the adult pattern may not be completely established until puberty. There do not appear to be substantive data for experimental species other than rats and mice, although the situation in humans appears similar in general outline and one may conclude that this pattern or some variant of it is characteristic of mammalian species in general.

Ontogeny of Phase II Enzymes

Phase II conjugating enzymes are generally less active in the neonate than the adult (Milsap and Jusko, 1994). Hence, there is concern that detoxification and elimination of chemicals is slower in infants. In humans, expression of some of the UGT enzymes matures to adult levels in two months after birth, although glucuronidation of some drugs by the UGT1A subfamily does not reach adult levels until puberty (Levy et al., 1975; Snodgrass, 1992; McCarver and Hines, 2002). Reduced glucuronidation in neonates slows the clearance of *N*-hydroxyarylamines, phenol, and benzene metabolites. Acetylation by the N-acetyltransferases and sulfation by sulfotransferases are generally somewhat comparable to adult levels, although it varies by tissue and by specific sulfotransferase (McCarver and Hines, 2002). Human glutathione sulfotransferase (GST) is present as a fetal isoform which decreases postnatally, while GST-alpha and GST-mu increase

over the first few years of life to adult levels (McCarver and Hines, 2002). Epoxide hydrolase, important in detoxifying reactive epoxide metabolites, is present in neonatal liver although at much reduced activity relative to adults (McCarver and Hines, 2002).

Clearances of Drugs in Infants and Children vs. Adults

Several investigators have evaluated age-related drug disposition (Renwick, 1998; Renwick et al., 2000; Ginsberg et al., 2002; Hattis et al., 2003). Renwick et al. (2000) noted higher internal doses in neonates and young infants versus adults for seven drugs that are substrates for glucuronidation, one with substrate specificity for CYP1A2, and four with substrate specificity for CYP3A4 metabolism. Ginsberg et al (2002) evaluated toxicokinetic information on 45 drugs in children and adults metabolized by different cytochrome P-450 pathways, by Phase II conjugations, or eliminated unchanged by the kidney. These authors noted half-lives 3-9-fold longer in infants than those in adults. It was also shown that the bulk of the elevated child/adult half-life ratios occurred primarily in the 0 to 6 month age range, and that for some compounds the clearance is actually higher in the 6 month to 2 year age grouping. In evaluating the interindividual variability by age, Hattis et al (2003) note that the largest interindividual variability occurs in the youngest children, apparently due to variability in development of critical metabolism and elimination pathways. Anderson and Holford (2008) noted that a comparison of three early-life drug clearance models (surface area, allometric ¾ power and per kilogram scaling) all demonstrated an increase in clearance over the first year of life due to the maturation of metabolic capacity.

Renal elimination depends on maturity of processes related to tubular reabsorption and secretion, and glomerular filtration rates. At birth, the glomerular filtration rate (GFR) is low (2-4 ml/min), increases in the first few days (8-20 ml/min) and slowly increases to adult values in 8-12 month old infants (Plunkett et al., 1992; Kearns et al, 2003).

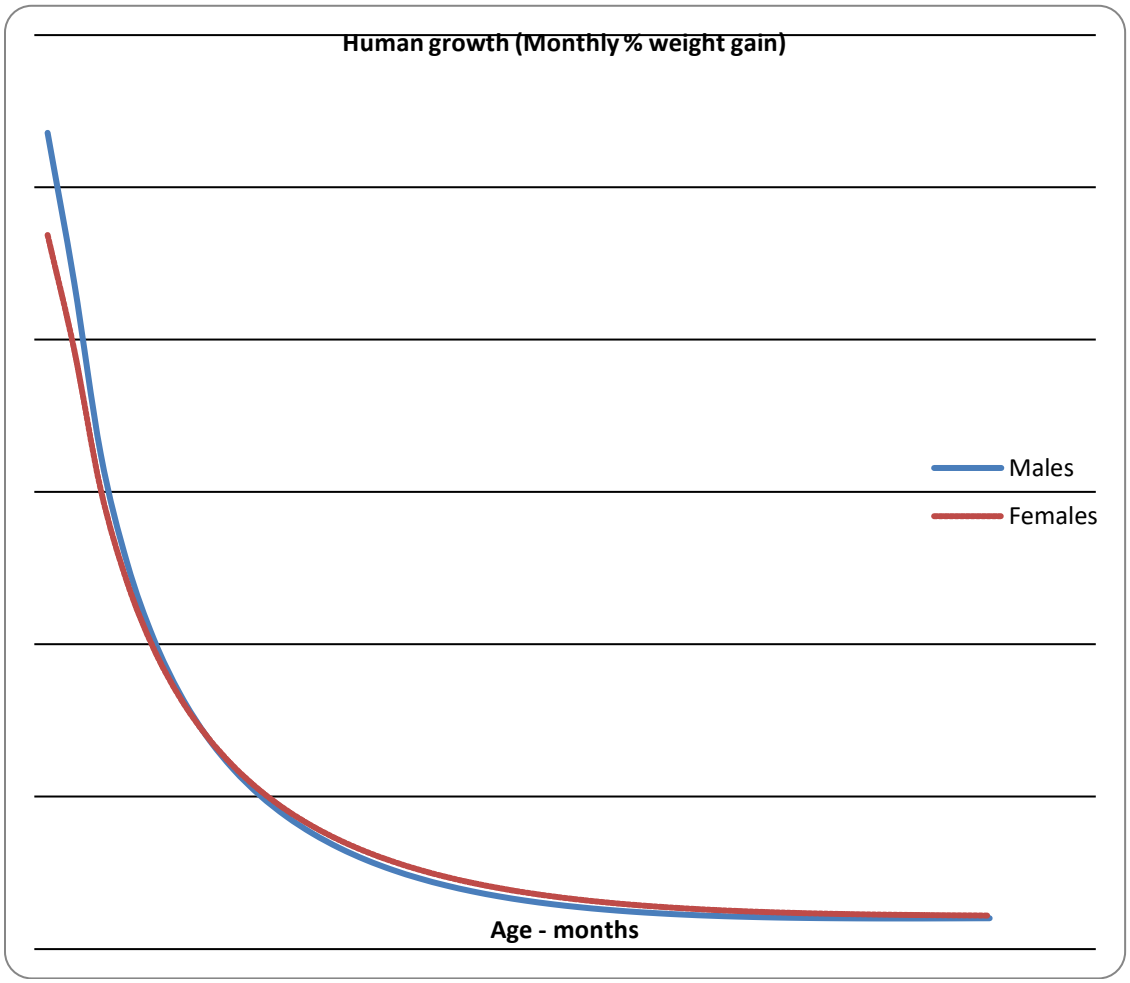
Newborn and young animals have less capacity to excrete chemicals into the bile than do adult animals. A number of chemicals are excreted more slowly via bile in neonates than adult rats, including ouabain, the glucuronide conjugate of sulfobromophthalein (Klaassen, 1973), and methyl mercury (Ballatori and Clarkson, 1982), resulting in a longer half-life in neonates.

Toxicodynamic Factors Relevant to Age Bins

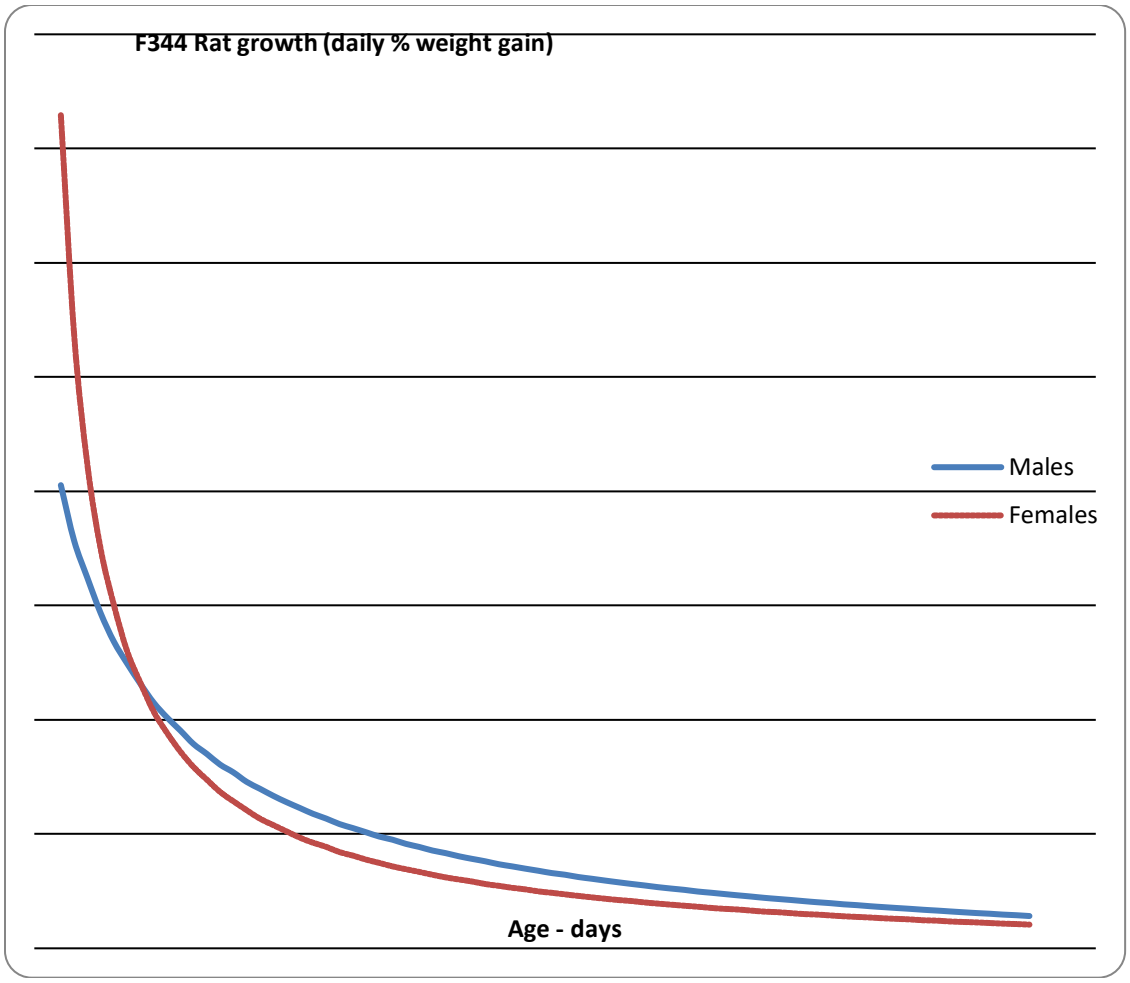
Important as the developmental changes in toxicokinetics are in determining sensitivity to carcinogens and other toxicants, it is likely that the toxicodynamic differences, *i.e.* intrinsic differences in susceptibility to carcinogenesis at the tissue or cellular level, are even more influential. Changes in cell division rates and differentiation, which are thought to be important toxicodynamic determinants of susceptibility to carcinogenesis, peak in the first 2 years of life for most major organ systems. Cell division continues to accommodate growth throughout childhood and adolescence, extending in some cases even into the young adult period in both humans and experimental animals. Adolescence is an important period for organ cell division and differentiation for the mammary gland and reproductive organs.

As noted above, one of the key factors influencing susceptibility to carcinogenesis is believed to be cell division rate, which acts both by forcing error-prone repair which fixes DNA damage as mutated gene sequences (McLean et al, 1982) and by promoting expansion of mutated clones

(Moolgavkar and Knudson, 1981). Actual cell division rates as a function of age are hard to determine for practical and (in the human case) ethical reasons. However, growth curves expressed as the proportional increment in body weight with time may be regarded as a reasonable although not perfect surrogate since for most tissues of the body cell size does not change markedly during growth. Both humans and rodents show remarkably high growth rates in infancy, which then drop steeply to a lower but still significant rate during childhood. A growth spurt at the beginning of adolescence is noticeable in its absolute magnitude, especially in males, but does not approach the proportional growth rate seen in infancy. The time intervals proposed to reflect the period of highest sensitivity to carcinogenesis (up to about 21 days in rodents, up to 24 months in humans) encompass the period of highest growth rate and thus it is assumed the highest cell division rates, as show in the following charts:



Data from CDC NHANES 2000:
http://www.cdc.gov/nchs/about/major/nhanes/growthcharts/datafiles.htm



Data from Tables A3 and A4 of Appendix J

Cell division rates in adult rodents and humans are harder to relate to growth curves since at least some tissues retain active cell division as part of their ongoing functionality and repair. In humans growth in body weight slows to essentially zero at the end of adolescence (and any later increments represent tissue specific changes such as increase in muscle or adipose tissue mass rather than overall growth). On the other hand, rodents continue to increase in body size (at a modest rate compared to that seen in earlier lifestages) throughout the adult period. However, it appears reasonable to conclude from the body weight data that an essentially adult pattern of overall cell division is established by the late adolescent period (age six weeks in rodents; 16 years in humans). However, increased cell division and cell differentiation are seen in the reproductive system and its accessories during puberty.

Organ Development

The age intervals chosen for the ASFs are generally supported by human organ system development data. Examples of supporting data are available for the lung, brain, immune system and liver. Zeltner and Burri (1987) stated that postnatal lung development consists of an alveolar stage, which lasts to about 1-1.5 years of age, and a stage of microvascular maturation, which exists from the first months after birth to the age of 2-3 years. Pinkerton and Joad (2006) describe

alveolar proliferation as occurring most prominently in the 0-2 year age range, with alveolar expansion continuing in the 2-8 year age range. Ballinoti et al. (2008) demonstrated that addition of alveoli rather than expansion is a major mode of lung growth in infants and toddlers by measuring a constant carbon monoxide diffusion capacity to lung volume from 3 through 23 months of age. Kajekar (2007) also considered the 0-2 age range to be the primary period of alveolar development, although there is continued cellular proliferation resulting in lung growth and expansion up to approximately 18 years of age.

Rice and Barone (2000) note that most of the cell proliferation phase of human radial glia and neuronal growth is finished by 2 years of age, based on evidence in Bayer et al. (1993). They note further that numerous studies have shown actively proliferating brain regions are more susceptible to anti-mitotic agents than the same structures after active proliferation ceases. Peak brain growth as a percentage of body weight occurs at birth and around post-natal day (PND) 7-8 in humans and rats, respectively (Watson *et al*., 2006). De Graaf-Peters and Hadders-Algra (2006) reviewed the ontogeny of the human central nervous system and found that a large amount of axon and dendrite sprouting and synapse formation and the major part of telencephalic myelination take place during the first year after birth. While the brain continues to remodel itself throughout life, cellular proliferation in the whole brain peaks by about one year of age and is relatively complete by age 2. Development of the blood-brain barrier (BBB) appears to continue in humans until approximately 6 months of age. Rat BBB functionality is essentially complete by approximately two weeks after birth (Watson *et al*., 2006).

The immune system development occurs in stages, primarily prenatally in primates and both pre- and post-natally in rodents (Dietert et al., 2000). Formation and expansion of hematopoetic stem cells is followed by expansion of lineage-specific stem cells, colonization of bone marrow and thymus, and maturation of cells to immunocompetence. In the primate, this is largely complete by 1 to 2 years of age (Holsapple et al., 2003), although establishment of immune memory develops throughout childhood and beyond. In the rodent, maturation to immunocompetence occurs postnatally from birth to about 30 days of age. In terms of carcinogenesis, perhaps one of the more important immune cells is the NK cell, thought to be responsible for immune surveillance and killing of circulating transformed cells. Based on immunohistochemistry, the principal cell lines including NK cells are present at gestation day 100 in the monkey and are at about 60% of adult values at birth (Holladay and Smialowicz, 2000).

As noted above, renal and hepatic clearance are both lower in humans at birth than in adults. Nephrogenesis is complete by 35 weeks gestation in humans and before birth in the mouse (but after birth in the rat). The ability to concentrate urine and the development of acid-base equilibrium appear in the first few months after birth (Zoetis and Hurtt, 2003). Renal clearance of drugs, a function of a number of processes in the kidney, appears to be comparable to adults within the first few months of life (Hattis et al., 2003; Ginsberg et al., 2002), while glomerular filtration, which rises rapidly over the first few postnatal months, is at adult values by two years of age (Zoetis and Hurtt, 2003). While complete anatomic maturity of the human liver is noted by 5 years of age (Walthall et al, 2005), liver function also appears to mature within the first year of life as seen by drug clearance studies cited above.

Critical Windows of Susceptibility to Carcinogens

It has been shown that there are critical windows during development both pre-and postnatally where enhanced susceptibility to carcinogenesis occurs (Anderson et al, 2000). Some of these observations relate to factors affecting the incidence of cancers in childhood, resulting from prenatal or preconception mutational events. For example, prenatal exposure to ionizing radiation and DES can result in leukemia and vaginal carcinoma, respectively, in childhood. Although obviously a source of great concern, these cancers appearing during childhood are relatively rare compared to cancers appearing later in life. Thus the concern in risk assessment for early in life exposures is to address the lifetime cancer incidence as a result of these exposures, including both cancers appearing during childhood and those appearing later.

OEHHA (see Appendix J) and other investigators (U.S. EPA, 2005; Barton et al, 2005; Hattis et al., 2004) have examined the available rodent data on sensitivity to carcinogenic exposures early in life. All these investigators found substantial increases in sensitivity to carcinogens in animal studies where exposures to young animals were compared to similar exposures to adults. Hattis et al. (2004) reported maximum likelihood estimates for the ratio of carcinogenic potency during the period from birth to weaning to the adult potency of between 8.7 and 10.5, whereas Barton et al (2005) reported a weighted geometric mean of 10.4 for the ratio of juvenile (less than 6-8 weeks) to adult potency in rodents. However, the number of experiments which provide information of this type, and the carcinogenic agents which have been studied, are relatively limited. Hattis examined several different datasets and study designs, but these covered only 13 different chemicals, while the mean value reported by Barton et al. was based on only six of the 18 chemicals which they examined. OEHHA's analysis included data in rodents on 23 chemicals, and found median potency ratios of 13.5 for the postnatal period (birth to day 22) and 4.5 for the juvenile period (postnatal days 22 to ~49) relative to adults (day ~49 to 2 years). These potency ratios include the adjustment for time to manifest tumor (*e.g.*, age to the power of three), unlike the earlier investigations. All these investigations identified variations in the observed lifetime potency ratio depending on the type of experimental design, the sex of the animals, the time of exposure and especially between chemicals. Nevertheless these analyses, although falling far short of a comprehensive evaluation of the age dependence of carcinogenic potency for all the chemicals of interest, do show a consistent overall trend of increasing potency for exposures early in life, especially soon after birth.

An evaluation of cancer induction by ionizing radiation also provides support for the concept of enhanced sensitivity to carcinogenesis at younger ages. Various studies of this phenomenon have been undertaken in animal models, but the important point for the present discussion is that epidemiological data exist which indicate age-dependent sensitivity in humans (U.S. EPA, 1994; 1999). The most extensive data set showing age-dependent effects is that for Japanese survivors of the atomic bomb explosions at Hiroshima and Nagasaki. Analysis of these data shows linear increases in tumor incidence at a number of sites with increasing radiation dose and younger age at exposure. There are other data suggesting humans are more susceptible to chemical carcinogens when exposure occurs in childhood. These data exist for tobacco smoke (Marcus et al., 2000; Wiencke et al., 1999) and chemotherapy and radiation (Mauch et al., 1996; Swerdlow et al., 2000; Franklin et al., 2006).

Proposed Age Bins for Application of Default Age Sensitivity Factors

In developing a default science-based risk assessment policy to address this general conclusion, one key variable to define is the age interval or intervals over which age-dependent sensitivity factors should be applied. Different investigators have considered different age ranges, but in general the more sensitive period has at least been defined as including the time from birth up to mid-adolescence when the major phases of growth and hormonal change are complete. It is also recognized that, apart from the dramatic prenatal developmental events, the earliest postnatal stages represent the greatest differences in physiology and biochemistry from the adult. This reflects the immaturity of many organ systems, extremely rapid growth, and the incomplete maturation of various metabolic capabilities. As noted earlier, the rodent age bins in OEHHA's analysis were based on gross developmental milestones (birth, weaning, sexual maturity). OEHHA's analysis of studies that included exposure sometime between birth and weaning indicated this period as having the highest sensitivity to carcinogenesis. The data for the later juvenile period (postnatal days 22 to ~ 49) are somewhat sparse, covering only three carcinogens and only one where there are corresponding data for both postnatal and juvenile lifestages. However, it appears based on the overall range of potency ratios observed for the juvenile period that sensitivity to many carcinogens is elevated in this period also, but to a lesser extent than during the first 22 days. [Hattis et al. (2005) and Barton et al. (2005) report analyses for exposures at any time during the juvenile period, i.e. up to 6-8 weeks, and do not separate by additional age bins].

Weaning is not such an obvious or consistently timed transition for humans, being subject to a wide range of cultural and economic variables. However, it is generally considered that the human infant period encompasses the first two years of life. This period includes the most rapid periods of cellular division and differentiation for the major organ systems (excluding the breast and reproductive organs). Although there is linear growth between 2 and 8 years of age, the organ development is largely although not entirely complete.

Thus, considering both the development of major organ systems and the associated differences in toxicodynamic and toxicokinetic factors, OEHHA initially proposed to apply the postnatal ASF derived from rodent studies (birth to 21 days) to the human age intervals of birth - < 2 years. Similarly, OEHHA chose to apply the "juvenile" ASF derived from rodent studies (22 - ~49 days) to the human ages 2 - < 16 years. This timetable was also selected by U.S. EPA (2005) in their supplemental guidance for assessing early-life susceptibility to carcinogens. They describe their choice of critical periods as follows:

> "The adjustments described below reflect the potential for early-life exposure to make a greater contribution to cancers appearing later in life. The 10-fold adjustment represents an approximation of the weighted geometric mean tumor incidence ratio from juvenile or adult exposures in the repeated dosing studies (see Table 8). This adjustment is applied for the first 2 years of life, when toxicokinetic and toxicodynamic differences between children and adults are greatest (Ginsberg et al., 2002; Renwick, 1998). Toxicokinetic differences from adults, which are greatest at birth, resolve by approximately 6 months to 1 year, while higher growth rates extend for longer periods. The 3-fold adjustment represents an intermediate level of adjustment that is applied after 2 years of age through <16 years of age. This upper age limit represents middle adolescence following the period of rapid developmental changes in puberty and the conclusion of growth in body height in

NHANES data (Hattis et al., 2005). Efforts to map the approximate start of mouse and rat bioassays (i.e., 60 days) to equivalent ages in humans ranged from 10.6 to 15.1 years (Hattis et al., 2005)."

There is general agreement that rodents are born at a maturational stage approximately equivalent to a third trimester human fetus. Thus, there is good rationale to include the third trimester of pregnancy in the age bin for application of the ASF of 10. Therefore, OEHHA is applying the ASF of 10 for exposures during the third trimester of pregnancy to age 2. The default ASF values used by OEHHA are summarized in Table 2.

While there is strong evidence that growth and therefore cell proliferation rates and cell differentiation are extremely high prior to age 2, and lower (although still elevated relative to the adult) thereafter, there is still residual uncertainty with respect to the cut point for application of the ASFs of 10 and 3. Thus, another possible approach would be to move the cut point for the application of the ASF of 10 to a later age to account for this uncertainty. We present the effect on risk estimates of varying cut points in Table 3 and Table 4.

Table 2. Default Age Sensitivity Factors to be used to estimate cancer risks to infants and children

R (third trimester to age 2yrs)	10
R (age 2 to age 16 yrs)	3
R (age 16 to 70 yrs)	1

Application of ASFs in Risk Assessment

The effect of using the proposed default ASFs in calculating cancer risk over a 70 year lifetime, and for a 9 year exposure common in the Hot Spots program risk assessments is demonstrated in Table 3 and Table 4 below. Ignoring for the moment the increased exposures to carcinogens that children experience, the effect of the weighting factors is to increase the lifetime cancer risk by about 2. For risks from shorter exposures, such as the commonly used 9 year exposure scenario, OEHHA proposes to evaluate risk from exposures starting at the third trimester in the surrounding general population. The weighting factors in this case increase the risk to a larger extent. Depending on the exposure scenario, the use of age-specific distributions for uptake rates for air, food and water would also increase the risk estimates significantly independent of any application of ASFs. This is because the uptake rates for all these media per unit of body weight are higher in children and, especially, infants.

Assessing risks to short-term exposures to carcinogens involves additional uncertainties. The cancer potency factors are generally based on long-term exposures. However, in reality, the local air districts in California are frequently assessing risk from short term activities related to construction, mitigation of contaminated soils, and so forth. OEHHA recommends that when assessing such shorter term projects, the districts assume a minimum of 2 years of exposure and apply the slope factors and the 10 fold ASF to such assessments. Exposure durations longer than 2 years would use the method for the remaining years as noted above.

Table 3. Example of default ASF use for a lifetime exposure (not adjusted for age-specific exposure)

Carcinogen Potency = 1 $(mg/kg\text{-}d)^{-1}$
Exposure = 0.0001 mg/kg-d
No consideration of differences of exposure

No adjustment: Lifetime Risk = potency × dose			Risk
70 year Lifetime risk = 1 × 0.0001			**1.0×10^{-4}**

With proposed default ASF of 10 for third trimester to age 2, and 3 for ages 2 to 16 years: LR = Σ (potency x dose x ASF x fraction of lifetime)	ASF	Duration	Risk
R (third trimester to age 2yrs)	10	2.25/70	0.321×10^{-4}
R (age 2 to age 16 yrs)	3	14/70	0.600×10^{-4}
R (age 16 to 70 yrs)	1	54/70	0.771×10^{-4}
70 year Lifetime Risk			**1.7×10^{-4}**

For comparison, if ASF of 10 were applied to age 5, and ASF of 3 for the ages 5 to 16 years: LR = Σ (potency x dose x ASF x fraction of lifetime)	ASF	Duration	Risk
R (birth to age 5)	10	5.25/70	0.750×10^{-4}
R (age 5 to 16 yrs)	3	11/70	0.471×10^{-4}
R (age 16 to 70 yrs)	1	54/70	0.771×10^{-4}
70 year Lifetime Risk			**2.0×10^{-4}**

Table 4. Example of default ASF use for a 9-year exposure

Carcinogen Potency = 1 $(mg/kg\text{-}d)^{-1}$
Exposure = 0.0001 mg/kg-d
No consideration of differences of exposure

No adjustment: Total Risk = potency × dose x fraction of lifetime		Duration	Risk
9-year Total Risk		9/70	**0.13×10^{-4}**
With default ASF of 10 for third trimester to age 2 and 3 thereafter: LR = Σ (potency x dose x ASF x fraction of lifetime)	ASF	Duration	Risk
R (third trimester to age 2yrs)	10	2.25/70	0.321×10^{-4}
R (age 2 to 9 yrs)	3	7/70	0.300×10^{-4}
9 year Total Risk			**0.62×10^{-4}**
For comparison, if ASF of 10 applied to age 5, and ASF of 3 thereafter: LR = Σ (potency x dose x ASF x fraction of lifetime)	ASF	Duration	Risk
R (birth to age 5 yrs)	10	5/70	0.750×10^{-4}
R (age 5 to 9 yrs)	3	4/70	0.171×10^{-4}
9 year Total Risk			**0.92×10^{-4}**

Special Consideration of Puberty

In addition to the general concerns over increased sensitivity to carcinogenesis during infancy and childhood, there are specific concerns for exposure during the period when hormonal and developmental changes associated with puberty are in process, especially for carcinogens with hormonal modes of action or with impacts on the reproductive system and its accessory organs. At puberty, there is increased development of breast and reproductive organs that clearly involves rapid cellular division and differentiation. Thus, for carcinogens that induce mammary and reproductive organ cancers, puberty represents a time of increased sensitivity. As noted in the section on Selection of Default Age-Sensitivity Factors (page 50), if the risk assessor is evaluating a chemical with the potential for more than usually enhanced potency during this period, such as those which induce mammary or reproductive organ tumors (*e.g.*, a polycyclic aromatic hydrocarbon), then the risk assessment may use a larger ASF to calculate risk from exposure during puberty. OEHHA may recommend chemical-specific ASFs for puberty to the local air quality management districts for use in the Air Toxics Hot Spots program.

U.S.EPA Analysis of the Effect of Age at Exposure on Cancer Potency

U.S. EPA addressed the potential for increased susceptibility to cancer caused by environmental chemicals when the exposure occurs during an early lifestage in "Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens" (U.S. EPA, 2005b) (referred to henceforth as the Supplemental Guidance). This document is intended to be a companion to the revised "Guidelines for Carcinogen Risk Assessment" (U.S. EPA, 2005a). We present a summary of their analysis, which supports the policy decision to weight cancer potency and therefore risk by age-at-exposure. As previously noted, there are several methodological differences between the U.S. EPA analysis and the OEHHA analysis. Of note, in the OEHHA analysis all treatment-related tumors that were observed in a given lifestage exposure experiment were taken into account in estimating cancer potency. Thus in comparing cancer potencies associated with early life vs. adult exposure, OEHHA compared the total cancer risk associated with exposure during a given lifestage, rather than comparing the risk for cancers at one single site in each lifestage, as the U.S. EPA did. In addition, the age groupings are somewhat different in the U.S. EPA analysis from those used by OEHHA in their analysis (described above). For example, prenatal (*in utero*) exposures were not part of the analysis performed by U.S. EPA, and that Agency's analyses did not distinguish between postnatal and juvenile exposures.

U.S. EPA oral exposure cancer risk methodology relies on estimation of the lifetime average daily dose, which can account for exposure factor differences between adults and children (*e.g.*, eating habits and body weight). However, early lifestage susceptibility differences have not been taken into consideration when cancer potency factors were calculated. The Supplemental Guidance document focused on studies that define the potential duration and degree of increased susceptibility that may arise from early-life exposures. An analysis of those studies including a detailed description of the procedures used was published in Barton *et al*. (2005) (included as Appendix I). The criteria used to decide if a study could be included in the quantitative analysis are as follows (excerpted from U.S. EPA, 2005b):

1. Exposure groups at different post-natal ages in the same study or same laboratory, if not concurrent (to control for a large number of potential cross-laboratory experimental variables including pathological examinations),
2. Same strain/species (to eliminate strain-specific responses confounding age-dependent responses),
3. Approximately the same dose within the limits of diets and drinking water intakes that obviously can vary with age (to eliminate dose-dependent responses confounding age-dependent responses),
4. Similar latency period following exposures of different ages (to control for confounding latency period for tumor expression with age-dependent responses), arising from sacrifice at >1 year for all groups exposed at different ages, where early-life exposure can occur up to about 7 weeks. Variations of around 10 to 20% in latency period are acceptable,
5. Postnatal exposure for juvenile rats and mice at ages younger than the standard 6 to 8 week start for bioassays; prenatal (*in utero*) exposures are not part of the current analysis. Studies that have postnatal exposure were included (without adjustment) even if they also involved prenatal exposure,

6. "Adult" rats and mice exposure beginning at approximately 6 to 8 weeks old or older, *i.e.* comparable to the age at initiation of a standard cancer bioassay (McConnell, 1992). Studies with animals only at young ages do not provide appropriate comparisons to evaluate age-dependency of response (*e.g.*, the many neonatal mouse cancer studies). Studies in other species were used as supporting evidence, because they are relatively rare and the determination of the appropriate comparison ages across species is not simple, and
7. Number of affected animals and total number of animals examined are available or reasonably reconstructed for control, young, and adult groups (i.e., studies reporting only percent response or not including a control group would be excluded unless a reasonable estimate of historical background for the strain was obtainable).

Cancer potencies were estimated from a one-hit model (a restricted form of the Weibull time-to-tumor model), which estimates cumulative incidence for tumor onset. U.S. EPA (2005b) compared the estimated ratio of the cancer potency from early-life exposure to the estimated cancer potency from adult exposure. The general form of the equation for the tumor incidence at a particular dose, [P(dose)] is:

$$P(dose) = 1-[1-P(0)]\exp(-\text{cancer potency}*\text{dose})$$

where P(0) is the incidence of the tumor in controls. The ratio of juvenile to adult cancer potencies at a single site were calculated by fitting this model to the data for each age group. The model fit depended upon the design of the experiment that generated the data. Studies evaluated by U.S. EPA had two basic design types: experiments in which animals were exposed either as juveniles or as adults (with either a single or multiple dose in each period), and experiments in which exposure began either in the juvenile or in the adult period, but once started, continued through life.

The model equations for the first study type are:

$$P_A = P_0 + (1-P_0)\,(1-e^{-m_A \delta_A})$$

$$P_J = P_0 + (1-P_0)\,(1-e^{-m_A e^{\lambda} \delta_J})$$

where A and J refer to the adult and juvenile period, respectively, λ is the natural logarithm of the juvenile:adult cancer potency ratio, P_0 is the fraction of control animals with the particular tumor type being modeled, P_x is the fraction of animals exposed in age period x with the tumor, m_A is the cancer potency, and δ_x is the duration or number of exposures during age period x.

The goal of the model is to determine λ, which is the logarithm of the estimated ratio of juvenile to adult cancer potencies. This serves as a measure of potential susceptibility for early-life exposure.

For the second study type, the model equations take into account that exposures that were initiated in the juvenile period continue through the adult period. The model equations for the fraction of animals exposed only as adults with tumors in this design are the same as in the first study type, but the fraction of animals whose first exposure occurred in the juvenile period is:

$$P_J = P_0 + (1\text{-}P_0)\,(1\text{-}e^{-m_A\, e^{\lambda\cdot(\delta_J - \delta_A)} - m_A\,\delta_A})$$

δ_J includes the duration of exposure during the juvenile period and the subsequent adult period.

Parameters in these models were estimated using Bayesian methods and all inferences about the ratios were based on the marginal posterior distribution of λ. A complete description of these procedures (including the potential effect of alternative Bayesian priors that were examined) was published in Barton *et al.* (2005) (Appendix I). This method produced a posterior mean ratio of the early-life to adult cancer potency, which is an estimate of the potential susceptibility of early-life exposure to carcinogens. Ratios of greater or less than one indicate greater or less susceptibility from early-life exposure, respectively.

U.S. EPA reviewed several hundred studies reporting information on 67 chemicals or complex mixtures that are carcinogenic via perinatal exposure. Eighteen chemicals were identified which had animal study designs involving early-life and adult exposures in the same experiment. Of those 18 chemicals, there were overlapping subsets of 11 chemicals involving repeated exposures during early postnatal and adult lifestages and 8 chemicals using acute exposures (usually single doses) at different ages. Those chemicals are listed in Table 5.

Table 5 Chemicals having animal cancer study data available with early-life and adult exposures in the same experiment.

Chemical	Study Type
Amitrole	repeat dosing
Benzidine	repeat dosing
Benzo[a]pyrene (BaP)	acute exposure
Dibenzanthracene (DBA)	acute exposure
Dichlorodiphenyltrichloroethane (DDT)	lifetime exposure, repeat dosing
Dieldrin	lifetime exposure, repeat dosing
Diethylnitrosamine (DEN)	acute exposure, lifetime exposure
Dimethylbenz[a]anthracene (DMBA)	acute exposure
Dimethylnitrosamine (DMN)	acute exposure
Diphenylhydantoin, 5,5-(DPH)	lifetime exposure, repeat dosing
Ethylnitrosourea (ENU)	acute exposure
Ethylene thiourea (ETU)	lifetime exposure, repeat dosing
3-Methylcholanthrene (3-MC)	repeat dosing
Methylnitrosourea (NMU)	acute exposure
Polybrominated biphenyls (PBBs)	lifetime exposure, repeat dosing
Safrole	lifetime exposure, repeat dosing
Urethane	acute exposure, lifetime exposure
Vinyl chloride (VC)	repeat dosing

U.S. EPA calculated the difference in susceptibility between early-life and adult exposure as the estimated ratio of cancer potency at specific sites from early-life exposure over the cancer potency from adult exposure for each of the studies that were determined qualitatively to have appropriate study designs and adequate data. The results were grouped into four categories: 1) mutagenic chemicals administered by a chronic dosing regimen to adults and repeated dosing in the early postnatal period (benzidine, diethylnitrosamine, 3-methylcholanthrene, safrole, urethane and vinyl chloride); 2) chemicals without positive mutagenicity data administered by a chronic dosing regimen to adults and repeated dosing in the early postnatal period (amitrole, dichlorodiphenyltrichloroethane (DDT), dieldrin, ethylene thiourea, diphenylhydantoin, polybrominated biphenyls); 3) mutagenic chemicals administered by an acute dosing regimen (benzo[*a*]pyrene, dibenzanthracene, diethylnitrosamine, dimethylbenzanthracene, dimethyl-nitrosamine, ethylnitrosourea, methylnitrosourea and urethane); 4) chemicals with or without positive mutagenicity data with chronic adult dosing and repeated early postnatal dosing.

The acute dosing animal cancer studies were considered qualitatively useful by U.S. EPA because they involve identical exposures with defined doses and time periods demonstrating that differential tumor incidences arise exclusively from age-dependent susceptibility. However, they

were not used to derive a quantitative cancer potency factor age adjustment, primarily because most of the studies used subcutaneous or intraperitoneal injection as a route of exposure. These methods have not been considered quantitatively relevant routes of environmental exposure for human cancer risk assessment by U.S. EPA, for reasons including the fact that these routes of exposure are expected to have a partial or complete absence of first pass metabolism which could affect potency estimates. Additionally, U.S. EPA decided that cancer potency estimates are usually derived from chronic exposures, and therefore, any adjustment to those potencies should be from similar exposures.

The repeated dosing studies with mutagenic chemicals using exposures during early postnatal and adult lifestages were used to develop a quantitative cancer potency factor age adjustment. Studies with repeated early postnatal exposure were included in the analysis even if they also involved earlier maternal and/or prenatal exposure, while studies addressing only prenatal exposure were not used in the analysis. The weighted geometric mean susceptibility ratio (juvenile to adult) for repeated and lifetime exposures in this case was 10.4 (range 0.12 – 111, 42% of ratios greater than 1).

USEPA suggests the use of age-dependent-adjustment factors (ADAF) for chemicals acting through a mutagenic mode of action., based on the results of the preceding analysis, which concluded that cancer risks generally are higher from early-life exposure than from similar exposure doses and durations later in life:

1. For exposures before 2 years of age (i.e., spanning a 2-year time interval from the first day of birth until a child's second birthday), a 10-fold ADAF.

2. For exposures between 2 and <16 years of age (i.e., spanning a 14-year time interval from a child's second birthday until their sixteenth birthday), a 3-fold ADAF.

3. For exposures after turning 16 years of age, no adjustment (ADAF=1).

The ADAF of 10 used for the 0 – 2 years of age range is approximately the weighted geometric mean cancer potency ratio from juvenile versus adult exposures in the repeated dosing studies. U.S. EPA considered this period to display the greatest toxicokinetic and toxicodynamic differences between children and adults. Data were not available to calculate a specific dose-response adjustment factor for the 2 to <16-year age range, so EPA selected an ADAF of 3 because it was half the logarithmic scale difference between the 10-fold adjustment for the first two years of life and no adjustment (*i.e.*, 1-fold) for adult exposure. The ADAF of 3 represents an intermediate level of adjustment applied after 2 years of age through <16 years of age. The upper age limit (16 years of age) reflects the end of puberty and the attainment of a final body height. U.S. EPA recognizes that the use of a weighted geometric mean of the available study data to develop an ADAF for cancer potencies may either overestimate or underestimate the actual early-life cancer potency for specific chemicals, and therefore emphasizes in the Supplemental Guidance that chemical-specific data should be used in preference to these default adjustment factors whenever such data are available.

U.S. EPA is recommending the ADAFs described above only for mutagenic carcinogens, because the data for non-mutagenic carcinogens were considered to be too limited and the modes of action

too diverse to use this as a category for which a general default adjustment factor approach can be applied. OEHHA considers this approach to be insufficiently health protective. There is no obvious reason to suppose that the toxicokinetics of non-mutagens would be systematically different from those of mutagens. It would also be inappropriate to assume by default that non-mutagenic carcinogens are assumed to need a toxicodynamic correction factor of 1. Most if not all of the factors that make individuals exposed to carcinogens during an early-lifestage potentially more susceptible than those individuals exposed during adulthood also apply to non-mutagenic carcinogen exposures (*e.g.*, rapid growth and development of target tissues, potentially greater sensitivity to hormonal carcinogens, differences in metabolism). It should also be noted that carcinogens that do not cause gene mutations may still be genotoxic by virtue of causing chromosomal damage. Additionally, many carcinogens do not have adequate data available for deciding on a specific mode of action, or do not necessarily have a single mode of action. For these reasons, OEHHA will apply the default cancer potency factor age adjustments described above to all carcinogens unless data are available which allow for the development of chemical-specific cancer potency factor age adjustments. In those cases, an agent-specific model of age dependence (based on observational or experimental data) might be used, or alternative (larger or smaller) adjustment factors and age ranges may be applied where understanding of the mechanism of action and target tissues makes this appropriate.

Other Source Documents for Cancer Risk Assessment Guidance

As noted previously, the cancer potencies and unit risks tabulated in this technical support document have been developed by various programs over a number of years. The methods used therefore necessarily varied according to the date of the assessment and the program responsible. The following section summarizes the sources and procedures most commonly applied, and their historical context where this is apposite.

United States Environmental Protection Agency (U.S. EPA)

The U.S. EPA was one of the first regulatory agencies to develop and apply cancer risk assessment methodology. Their guidance documents and technical publications have been influential for many programs, including the California Air Toxics (Toxic Air Contaminants and Hot Spots) programs.

Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1986)

Prior to the more recent guidelines updating project which, after nearly ten years of internal and public review drafts culminated in the 2005 final revision (see below), U.S. EPA carcinogen risk assessment procedures were generally as described in Anderson *et al*. (1983) and "Guidelines for Carcinogen Risk Assessment" (U.S. EPA, 1986). These methods, which are outlined below, were used to calculate the Integrated Risk Information System (IRIS) cancer potency values, some of which are cited in this document. U.S. EPA has always indicated that cancer risk estimates based on adequate human epidemiologic data are preferred if available over estimates based on animal data. Although the newer guidelines offer alternative methods for dose-response analysis of animal bioassays, and updated consideration of specific topics such as lifestage-related differences in sensitivity, and mechanism of action for some types of carcinogen, the underlying principles and many of the specific procedures developed in these original guidelines are still applicable and in use.

U.S. EPA Calculation of Carcinogenic Potency Based on Animal Data

In extrapolating low-dose human cancer risk from animal carcinogenicity data, it is generally assumed that most agents that cause cancer also damage DNA, and that the quantal type of biological response characteristic of mutagenesis is associated with a linear non-threshold dose-response relationship. U.S. EPA stated that the risk assessments made with this model should be regarded as conservative, representing the most plausible upper limit for the risk. The mathematical expression used by U.S. EPA in the 1986 guidelines to describe the linear non-threshold dose-response relationship at low doses is the linearized multistage procedure developed by Crump (1980). This model is capable of fitting almost any monotonically increasing dose-response data, and incorporates a procedure for estimating the largest possible linear slope at low extrapolated doses that is consistent with the data at all experimental dose levels. A description of the linearized multistage procedure has been provided above (page 29). U.S. EPA used an updated version (GLOBAL86, Howe *et al*., 1986) of the computer program GLOBAL79 developed by Crump and Watson (1979) to calculate the point estimate and the 95% upper confidence limit of the extra risk $A(d)$.

U.S. EPA separated tumor incidence data according to organ sites or tumor types. The incidence of benign and malignant tumors was combined whenever scientifically defensible. U.S. EPA considered this incidence combination scientifically defensible unless the benign tumors are not considered to have the potential to progress to the associated malignancies of the same histogenic origin. The primary comparison in carcinogenicity evaluation is tumor response in dosed animals as compared to contemporary matched control animals. However, U.S. EPA stated that historical control data could be used along with concurrent control data in the evaluation of carcinogenic responses, and notes that for the evaluation of rare tumors, even small tumor responses may be significant compared to historical data. If several data sets (dose and tumor incidence) are available (different animal species, strains, sexes, exposure levels, exposure routes) for a particular chemical, the data set used in the model was the set where the incidence is statistically significantly higher than the control for at least one test dose level and/or where the tumor incidence rate shows a statistically significant trend with respect to dose level. The data set generating the highest lifetime cancer risk estimate (q_1^*) was chosen where appropriate. An example of an inappropriate data set would be a set which generates an artifactually high risk estimate because of a very small number of animals used. If there are 2 or more data sets of comparable size for a particular chemical that are identical with respect to species, strain, sex and tumor sites, the geometric mean of q_1^* estimated from each of those data sets was used for risk estimation. U.S. EPA assumed that mg/surface area/day is an equivalent dose between species. Surface area was further assumed to be proportional to the 2/3 power of the weight of the animal in question. Equivalent dose was therefore computed using the following relationship:

$$d = \frac{l_e * m}{L_e * W^{2/3}}$$

where L_e = experimental duration, l_e = exposure duration, m = average dose (mg/day) and W = average animal weight. Default average body weights for humans, rats and mice are 70, 0.35 and 0.03 kg, respectively.

Exposure data expressed as ppm in the diet were generally converted to mg/day using the relationship m = ppm * F * r, where ppm is parts per million of the chemical in the diet, F is the weight of the food consumed per day in kg, and r is the absorption fraction (assumed to be 1 in the absence of data indicating otherwise). The weight of food consumed, calories required, and animal surface area were generally all considered to be proportional to the 2/3 power of the animal weight, so:

$$m \propto \text{ppm} * W^{2/3} * r, \text{ or } \quad \frac{m}{rW^{2/3}} \propto \text{ppm}$$

The relationship could lead to the assumption that dietary ppm is an equivalent exposure between species. However, U.S. EPA did not believe that this assumption is justified, since the calories/kg food consumed by humans is significantly different from that consumed by laboratory animals (primarily due to differences in moisture content). An empirically derived food factor, $f = F/W$

was used, which is the fraction of a species' body weight consumed per day as food. U.S. EPA (1986) gave the *f* values for humans, rats and mice as 0.028, 0.05 and 0.13, respectively.

Dietary exposures expressed as concentrations in ppm were converted to mg/surface area using the following relationship:

$$\frac{m}{r * W^{2/3}} = \frac{\text{ppm} * F}{W^{2/3}} = \frac{\text{ppm} * f * W}{W^{2/3}} = \text{ppm} * f * W^{2/3}$$

Exposures expressed as mg/kg/day ($m/Wr = s$) were converted to mg/surface area using the relationship:

$$\frac{m}{rW^{2/3}} = s * W^{2/3}$$

The calculation of dose when exposure is via inhalation was performed for cases where 1) the chemical is either a completely water-soluble gas or aerosol and is absorbed proportionally to the amount of inspired air, or 2) where the chemical is a partly water-soluble gas which reaches an equilibrium between the inspired air and body compartments. After equilibrium is attained, the rate of absorption is proportional to metabolic rate, which is proportional to the rate of oxygen consumption, which is related to surface area.

Exposure expressed as mg/day to completely water-soluble gas or aerosols can be calculated using the expression $m = I * v * r$, where I is the inspiration rate/day in m^3, v is the concentration of the chemical in air (mg/m^3), and r is the absorption fraction (assumed to be the same for all species in the absence of data to the contrary; usually 1). For humans, the default inspiration rate of 20 m^3 has been adopted. Inspiration rates for 113 g rats and 25 g mice have been reported to be 105 and 34.5 liters/day, respectively. Surface area proportionality can be used to determine inspiration rate for rats and mice of other weights; for mice, $I = 0.0345\ (W / 0.025)^{2/3}$ m^3/day; for rats, $I = 0.105\ (W / 0.113)^{2/3}$ m^3/day. The empirical factors for air intake/kg/day (i) for humans, rats and mice are 0.29, 0.64 and 1.3, respectively. Equivalent exposures in mg/surface area can be calculated using the relationship:

$$\frac{m}{W^{2/3}} = \frac{Ivr}{W^{2/3}} = \frac{iWvr}{W^{2/3}} = iW^{1/3}vr$$

Exposure expressed as mg/day to partly water-soluble gases is proportional to surface area and to the solubility of the gas in body fluids (expressed as an absorption coefficient r for that gas). Equivalent exposures in mg/surface area can be calculated using the relationships $m = kW^{2/3} * v * r$, and $d = m/W^{2/3} = kvr$. The further assumption is made that in the case of route-to-route extrapolations (*e.g.*, where animal exposure is via the oral route, and human exposure is via inhalation, or vice versa), unless pharmacokinetic data to the contrary exist, absorption is equal by either exposure route.

Adjustments were made for experimental exposure durations shorter than the lifetime of the test animal; the slope q_1^* was increased by the factor $(L/L_e)^3$, where L is the normal lifespan of the experimental animal and L_e is the duration of the experiment. This assumed that if the average dose d is continued, the age-specific rate of cancer will continue to increase as a constant function of the background rate. Since age-specific rates for humans increase by at least the 2nd power of the age, and often by a considerably higher power (Doll, 1971), there is an expectation that the cumulative tumor rate, and therefore q_1^*, will increase by at least the 3rd power of age. If the slope q_1^* is calculated at age L_e, it would be expected that if the experiment was continued for the full lifespan L at the same average dose, the slope q_1^* would have been increased by at least $(L/L_e)^3$.

U.S. EPA Calculation of Carcinogenic Potency Based on Human Data

U.S. EPA stated that existing human epidemiologic studies with sufficiently valid exposure characterization are always used in evaluating the cancer potency of a chemical. If they showed a carcinogenic effect, the data were analyzed to provide an estimate of the linear dependence of cancer rates on lifetime cancer dose (equivalent to the factor q_1^*). If no carcinogenic effect was demonstrated and carcinogenicity had been demonstrated in animals, then it was assumed that a risk does exist, but it is smaller than could have been observed in the epidemiologic study. An upper limit of cancer incidence was calculated assuming that the true incidence is just below the level of detection in the cohort studied, which is largely determined by the cohort size. Whenever possible, human data are used in preference to animal data. In human epidemiologic studies, the response is measured as the relative risk of the exposed cohort of individuals compared to the control group. The excess risk ($R(X)$ - 1, where $R(X)$ is relative risk) was assumed to be proportional to the lifetime average exposure X, and to be the same for all ages. The carcinogenic potency is then equal to $[R(X) - 1]/X$ multiplied by the lifetime risk at that site in the general population. According to this original procedure, the confidence limit for the excess risk was not usually calculated. This decision was ascribed to the difficulty in accounting for inherent uncertainty in the exposure and cancer response data. More recent assessments have taken the opposite view and attempted to calculate and characterize this uncertainty by determining confidence limits, *inter alia*.

Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005a)

U.S. EPA revised its "Guidelines for Carcinogen Risk Assessment" (referred to henceforth as the "U.S. EPA Guidelines") in 2005. Compared to the 1986 version of this document, more emphasis is placed on establishing a "mode of action" (MOA). The following excerpt provides a definition of this term:

> "The term "mode of action" is defined as a sequence of key events and processes, starting with interaction of an agent with a cell, proceeding through operational and anatomical changes, and resulting in cancer formation. A "key event" is an empirically observable precursor step that is itself a necessary element of the mode of action or is a biologically based marker for such an element. Mode of action is contrasted with "mechanism of action," which implies a more detailed understanding and description of events, often at the molecular level, than is meant by mode of action".

Cancer risk assessments performed under the prior U.S. EPA Guidelines sometimes included a MOA description. However, the 1986 U.S. EPA Guidelines did not explicitly mandate the development of a MOA description in cancer risk assessments.

The MOA information is then used to govern how a cancer risk assessment shall proceed. Tumor incidence data sets arising from a MOA judged to be not relevant to humans are not used to extrapolate a cancer potency factor. If an MOA cannot be determined or is determined to have a low-dose linear dose-response and a nonmutagenic MOA, then a linear extrapolation method is used to develop a cancer potency factor. The same linear extrapolation is used for all lifestages, unless chemical specific information on lifestage or population sensitivity is available. Carcinogens that act via an MOA judged to have a nonlinear low-dose dose response are modeled using MOA data, or the RfD/RfC risk assessment method is used as a default. Adjustments for susceptible lifestages or populations are to be performed as part of the risk assessment process.

If a carcinogen is deemed to act via a mutagenic MOA, then the data from the MOA analysis is evaluated to determine if chemical-specific differences between adults and juveniles exist and can be used to develop a chemical-specific risk estimate incorporating lifestage susceptibility. If this cannot be done, then early-life susceptibility is assumed, and age-dependent adjustment factors (ADAFs) are applied as appropriate to develop risk estimates. In cases where it is not possible to develop a toxicokinetic model to perform cross-species scaling of animal tumor data sets which arise from oral exposures, the U.S. EPA Guidelines state that administered doses should be scaled from animals to humans on the basis of equivalence of $mg/kg^{3/4}$-d (milligrams of the agent normalized by the 3/4 power of body weight per day). This is a departure from the 1986 U.S. EPA guidelines, which used a 2/3 power of body weight normalization factor. Other adjustments for dose timing, duration and route are generally assumed to be handled in similar fashion to that described for the 1986 guidelines, although of course updated parameter values would be used where available.

The 2005 U.S. EPA Guidelines also use benchmark dose methodology (described above, page 27) to develop a "point-of departure" (POD) from tumor incidence data. For linear extrapolation, the POD is used to calculate a cancer potency factor, and for nonlinear extrapolation the POD is used in the calculation of a reference dose (RfD) or reference concentration (RfC).

It should be noted that none of the cancer potency factors listed in this document were obtained from U.S. EPA risk assessments performed under the 2005 U.S. EPA Guidelines. All U.S. EPA IRIS cancer potency values contained in this document were obtained from risk assessments using the 1986 U.S. EPA Guidelines.

Office of Environmental Health Hazard Assessment (OEHHA), California Environmental Protection Agency

The cancer risk assessment procedures originally used by the Office of Environmental Health Hazard Assessment (OEHHA) are outlined in "Guidelines for Chemical Carcinogen Risk Assessments and their Scientific Rationale" (referred to below as the Guidelines) (CDHS, 1985). These procedures were generally used in generating Toxic Air Contaminant (TAC) cancer potency values, standard Proposition 65 cancer potency values and Public Health Goal (PHG) cancer

potency values. Expedited Proposition 65 cancer potency values depart somewhat from those procedures and are discussed separately below.

OEHHA cancer risk assessment methodology as described by CDHS (1985) generally resembled that used at that time by U.S. EPA (Anderson *et al*., 1983; U.S. EPA, 1986). OEHHA risk assessment practice similarly reflects the evolution of the technical methodology (*e.g.*, as described in U.S. EPA, 2005a) since the original guidelines were published. The basic principles and procedures described below are still considered applicable. More recent additions to OEHHA cancer risk assessment methods such as the use of benchmark dose methodologies and early-lifestage cancer potency adjustments are discussed above. The Guidelines state that both animal and human data, when available, should be part of the dose-response assessment.

OEHHA Calculation of Carcinogenic Potency Based on Animal Data

The procedures used to extrapolate low-dose human cancer risk from animal carcinogenicity data assumed that a carcinogenic change induced in a cell is transmitted to successive generations of cell descendants, and that the initial change in the cell is an alteration (*e.g.*, mutation, rearrangement, etc.) in the cellular DNA. Non-threshold models are used to extrapolate to low-dose human cancer risk from animal carcinogenicity data.

Several models were proposed for extrapolating low-dose human cancer risk from animal carcinogenicity data in the original Guidelines. These models include the Mantel-Bryan method (log-probit model), the one-hit model, the linearized multistage procedure, the gamma multihit model, and a number of time-to-tumor models. The Guidelines stated that time-to-tumor models (i.e., a Weibull-in-time model) should be used for low-dose extrapolation in all cases where supporting data are available, particularly when survival is poor due to competing toxicity. However, the Guidelines also noted the difficulty of determining the actual response times in an experiment. Internal tumors are generally difficult to detect in live animals and their presence is usually detected only at necropsy. Additionally, use of these models often requires making the determination of whether a tumor was the cause of death, or was found only coincidentally at necropsy when death was due to other causes. Further, competing causes of death, such as chemical toxicity, may decrease the observed time-to-tumor for nonlethal cancers by allowing earlier necropsy of animals in higher dose groups. The linearized multistage (LMS) procedure was noted as being an appropriate method for dose extrapolation in most cases, with the primary exception being a situation in which sufficient empirical data are available to indicate a dose-response curve of a "quasi-threshold" type (*e.g.*, flat for two or three dose levels, then curving sharply upwards). In this case, the LMS procedure may underestimate the number of stages and overestimate the low-dose risks. In this case, the gamma multihit model was suggested as being a potential alternative. The Mantel-Bryan model was described as having little biological basis as applied to carcinogenesis, and being likely to underestimate risks at low doses. The Guidelines stated that this model should not be used for low dose extrapolation. More recent practice has departed from these original guidelines in some respects, for instance by experimenting with cell-proliferation based models in a few cases. However, the LMS model remained the preferred extrapolation model for most purposes. Some of the difficulties in achieving a satisfactory fit to tumor incidence data were found to be alleviated by application of toxicokinetic models and use of an internal rather than applied dose metric with the LMS model. This has resulted in the alternative models originally advocated (Gamma multihit, Mantel-Bryan) being mostly

abandoned. As noted above (Dose-Response Assessment, page 23), the use of allegedly biologically based statistical models such as LMS has fallen from favor in recent years, and benchmark dose methodology has become the preferred method for extrapolating cancer potency values from animal cancer incidence data. However, it should also be noted that results generated by the LMS model and benchmark dose methodology from the same data set are often quite similar.

The 1985 Guidelines stated that both animal and human data, when available, should be part of the dose-response assessment. Although preference was given to human data when these were of adequate quality, animal studies may provide important supporting evidence. Low-dose extrapolation of human cancer risk from animal carcinogenicity data was generally based on the most sensitive site, species and study demonstrating carcinogenicity of a particular chemical, unless other evidence indicates that the data set in question is not appropriate for use. Where both benign and malignant tumors are induced at the same site and the benign tumors are considered to have the potential to progress to malignant tumors, the incidence data for both types of tumors could be combined to form the basis for risk assessment. Pharmacokinetic data on chemical metabolism, effective dose at target site, or species differences between laboratory test animals and humans were considered in dose-response assessments when available. In performing exposure scaling from animals to humans, the "surface area" correction (correcting by the 2/3 power of body weight) was used unless specific data indicate that this should not be done. The Guidelines assumed that in the absence of evidence to the contrary, chemicals that cause cancer after exposure by ingestion will also cause cancer after exposure by inhalation, and vice versa. These original proposals have continued in use with little change except that currently, TAC and PHG cancer potency factor calculations use a 3/4 power of body weight correction for interspecies scaling, in line with current U.S. EPA practice. The standard Proposition 65 cancer potency factor calculations still use a 2/3 power correction because the cancer potency calculation method is specified in regulation (California Health and Safety Code 25249.5 *et seq*.).

Cancer unit risk factors [in units of $(\mu g/m^3)^{-1}$] have been calculated from cancer potency factors [in units of $(mg/kg\text{-}day)^{-1}$] using the following relationship:

$$UR = \frac{CPF * 20\ m^3}{70\ kg\ *\ CV}$$

where UR is the cancer unit risk, CPF is the cancer potency factor, 70 kg is the reference human body weight, 20 m^3 is the reference human inspiration rate/day, and CV is the conversion factor from mg to µg (= 1000). The cancer unit risk describes the excess cancer risk associated with an inhalation exposure to a concentration of 1 $\mu g/m^3$ of a given chemical; the cancer potency factor describes the excess cancer risk associated with exposure to 1 mg of a given chemical per kilogram of body weight.

It should be noted that although this default method is still used in deriving published cancer unit risk values, for site-specific risk assessments age-appropriate distributions and percentile values are used in the current version of the Hot Spots exposure assessment document. Where exposure to children occurs (as it does in most exposures to the general population surrounding a source

site) it is also necessary to apply the age-specific adjustment factors for the appropriate durations in accordance with the guidance offered above (Page 30 *et seq.*).

OEHHA Calculation of Carcinogenic Potency Based on Human Data

Human epidemiologic studies with adequate exposure characterization are used to evaluate the cancer potency of a chemical. If they show a carcinogenic effect, the data are analyzed to provide an estimate of the linear dependence of cancer rates on lifetime cancer dose. The 1985 Guidelines stated that with continuous exposure, age-specific incidence continues to increase as a power function (*e.g.*, t^3 or t^4) of the elapsed time since initial exposure. Lifetime risks can be estimated by applying such a power function to the observed data and extrapolating beyond the actual followup period. OEHHA has generally undertaken the calculation of study power and confidence bounds on the potency estimate as important tools to establish the credibility of the estimate obtained and in comparing this with other estimates (from other human studies or from animal data). Due to the diversity in quality and type of epidemiological data, the specific approaches used in OEHHA risk assessments based on human epidemiologic studies vary on a case by case basis rather than following explicit general guidelines. Examples of the methods used can be observed in the Toxic Air Contaminant documents (these documents are listed in Appendix D: the methods used are described in the compound summaries provided in Appendix B).

Expedited Proposition 65 Cancer Risk Assessment Methodology

Expedited cancer potency values developed for several agents listed as carcinogens under Proposition 65 (California Health and Safety Code 25249.5 *et seq*.) were derived from selected animal carcinogenicity data sets of the Carcinogenic Potency Database (CPDB) of Gold *et al.* (1984, 1986, 1987, 1989, 1990, 1997) using default procedures specified in the administrative regulations for Proposition 65 (Title 22 California Code of Regulations [CCR] 12703). OEHHA hazard assessments usually describe all relevant data on the carcinogenicity (including dose-response characteristics) of the chemical under examination, followed by an evaluation of any pharmacokinetic and mechanistic (*e.g.*, genotoxicity) data. An evaluation of the data set for the chemical may indicate that adjustments in target dose estimates or use of a dose response model different from the default are appropriate. The procedure used to derive expedited Proposition 65 cancer potency values differs from the usual methodology in two ways. First, it relies on cancer dose response data evaluated and extracted from the original literature by Gold *et al.* Second, the choice of a linearized multistage procedure for generating cancer potency values is automatic, and pharmacokinetic adjustments are not performed. The methods used to develop expedited cancer potency values incorporate the following assumptions:

1. The dose response relationship for carcinogenic effects in the most sensitive species tested is representative of that in humans.
2. Observed experimental results can be extrapolated across species by use of the interspecies factor based on "surface area scaling."
3. The dose to the tissue giving rise to a tumor is assumed to be proportional to the administered dose.
4. The linearized multistage polynomial procedure can be used to extrapolate potency outside the range of experimental observations to yield estimates of "low" dose potency.

5. Cancer risk increases with the third power of age.

The Carcinogenic Potency Database of Gold *et al.* (1984, 1986, 1987, 1989, 1990) contains the results of more than 4000 chronic laboratory animal experiments on 1050 chemicals by combining published literature with the results of Federal chemical testing programs (Technical Reports from the Carcinogenesis Bioassay Program of the National Cancer Institute (NCI)/National Toxicology Program (NTP) published prior to June 1987). The published literature was searched (Gold *et al*., 1984) through the period December 1986 for carcinogenicity bioassays; the search included the Public Health Service publication "Survey of Compounds Which Have Been Tested for Carcinogenic Activity" (1948-1973 and 1978), monographs on chemical carcinogens prepared by the International Agency for Research on Cancer (IARC) and Current Contents. Also searched were Carcinogenesis Abstracts and the following journals: British Journal of Cancer, Cancer Letters, Cancer Research, Carcinogenesis, Chemosphere, Environmental Health Perspectives, European Journal of Cancer, Food and Chemical Toxicology, Gann, International Journal of Cancer, Journal of Cancer Research and Clinical Oncology (formerly Zeitschrift fur Krebsforschung und Klinische Onkologie), Journal of Environmental Pathology and Toxicology, Journal of Toxicology and Environmental Health, Journal of the National Cancer Institute, and Toxicology and Applied Pharmacology. Studies were included in the database if they met the following conditions:

1. The test animals were mammals.
2. Chemical exposure was started early in life (100 days of age or less for hamsters, mice and rats).
3. Route of administration was via the diet, drinking water, gavage, inhalation, intravenous injection or intraperitoneal injection.
4. The test chemical was administered alone (not in combination with other chemicals).
5. Chemical exposure was chronic (*i.e*. duration of exposure was at least one-fourth the standard lifespan for that species), with not more than 7 days between exposures.
6. The experiment duration was at least half the standard lifespan for the species used.
7. The study design included a control group and at least 5 animals/exposure group.
8. No surgical interventions were performed.
9. Pathology data were reported for the number of animals with tumors (not total number of tumors).
10. All results reported were original data (not analysis of data reported by other authors).

Included in their data set tabulations are estimates of average doses used in the bioassay, resulting tumor incidences for each of the dose levels employed for sites where significant responses were observed, dosing period, length of study and histopathology. Average daily dose levels were calculated assuming 100% absorption. Dose calculations follow procedures similar to those of Cal/EPA and U.S. EPA; details on methods used and standard values for animal lifespans, body weights, and diet, water and air intake are listed in Gold *et al.* (1984). OEHHA (1992) reviewed the quality assurance, literature review, and control procedures used in compiling the data and found them to be sufficient for use in an expedited procedure. Cancer potency estimates were

derived by applying the mathematical approach described in the section below to dose response data in the Gold *et al.* database.

The following criteria were used for data selection:

1. Data sets with statistically significant increases in cancer incidence with dose ($p \leq 0.05$) were used. (If the authors of the bioassay report considered a statistically significant result to be unrelated to the exposure to the carcinogen, the associated data set was not used.)
2. Data sets were not selected if the endpoint was specified as "all tumor-bearing animals" or results were from a combination of unrelated tissues and tumors.
3. When several studies were available, and one study stood out as being of higher quality due to numbers of dose groups, magnitude of the dose applied, duration of study, or other factors, the higher quality study was chosen as the basis for potency calculation if study results were consistent with those of the other bioassays listed.
4. When there were multiple studies of similar quality in the sensitive species, the geometric mean of potencies derived from these studies was taken. If the same experimentalists tested two sexes of the same species/strain under the same laboratory conditions, and no other adequate studies were available for that species, the data set for the more sensitive sex was selected.
5. Potency was derived from data sets that tabulate malignant tumors, combined malignant and benign tumors, or tumors that would have likely progressed to malignancy.

Cancer potency was defined as the slope of the dose response curve at low doses. Following the default approach, this slope was estimated from the dose response data collected at high doses and assumed to hold at very low doses. The Crump linearized multistage polynomial (Crump *et al.*, 1977) was fit to animal bioassay data:

$$\text{Probability of cancer} = 1 - \exp[-(q_0 + q_1 d + q_2 d^2 + ...)]$$

Cancer potency was estimated from the upper 95% confidence bound on the linear coefficient q_1, which is termed q_1^*.

For a given chemical, the model was fit to a number of data sets. As discussed in the section above, the default was to select the data for the most sensitive target organ in the most sensitive species and sex, unless data indicated that this was inappropriate. Deviations from this default occur, for example, when there are several bioassays or large differences exist between potency values calculated from available data sets.

Carcinogenicity bioassays using mice and/or rats will often use an exposure duration of approximately two years. For standard risk assessments, this is the assumed lifespan for these species. Animals in experiments of shorter duration are at a lower risk of developing tumors than those in the standard bioassay; thus potency is underestimated unless an adjustment for experimental duration is made. In estimating potency, short duration of an experiment was taken into account by multiplying q_1^* by a correction factor equal to the cube of the ratio of the assumed standard lifespan of the animal to the duration of the experiment (T_e). This assumes that the cancer hazard would have increased with the third power of the age of the animals had they lived longer:

$$q_{animal} = q_1^* * (104 \text{ weeks}/T_e)^3$$

In some cases excess mortality may occur during a bioassay, and the number of initial animals subject to late occurring tumors may be significantly reduced. In such situations, the above described procedure can, at times, significantly underestimate potency. A time-dependent model fit to individual animal data (i.e., the data set with the tumor status and time of death for each animal under study) may provide better potency estimates. When Gold *et al.* indicated that survival was poor for a selected data set, a time-dependent analysis was attempted if the required data were available in the Tox Risk (Crump *et al.*, 1991) data base. The Weibull multistage model (Weibull-in-time; multistage-in-dose) was fit to the individual animal data.

To estimate human cancer potency, q_{animal} values derived from bioassay data were multiplied by an interspecies scaling factor (K; the ratio of human body weight (bw_h) to test animal body weight (bw_a), taken to the 1/3 power (Anderson *et al.*, 1983)):

$$K = (bw_h/bw_a)^{1/3}$$

Thus, cancer potency = $q_{human} = K * q_{animal}$

Chemical-specific Descriptions of Cancer Potency Value Derivations

Unit Risk and potency values for chemicals whose cancer potency values were obtained from Toxic Air Contaminant documents, standard or expedited Proposition 65 documents, U.S. EPA's Integrated Risk Information System (IRIS) documents and Health Effects Assessment Summary Table (HEAST) entries, or from other documents prepared by OEHHA's Air Toxicology and Epidemiology Branch or Pesticide and Environmental Toxicology Branch are presented in Appendix A. Information summaries for these chemicals are presented in Appendix B.

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Exhibit H

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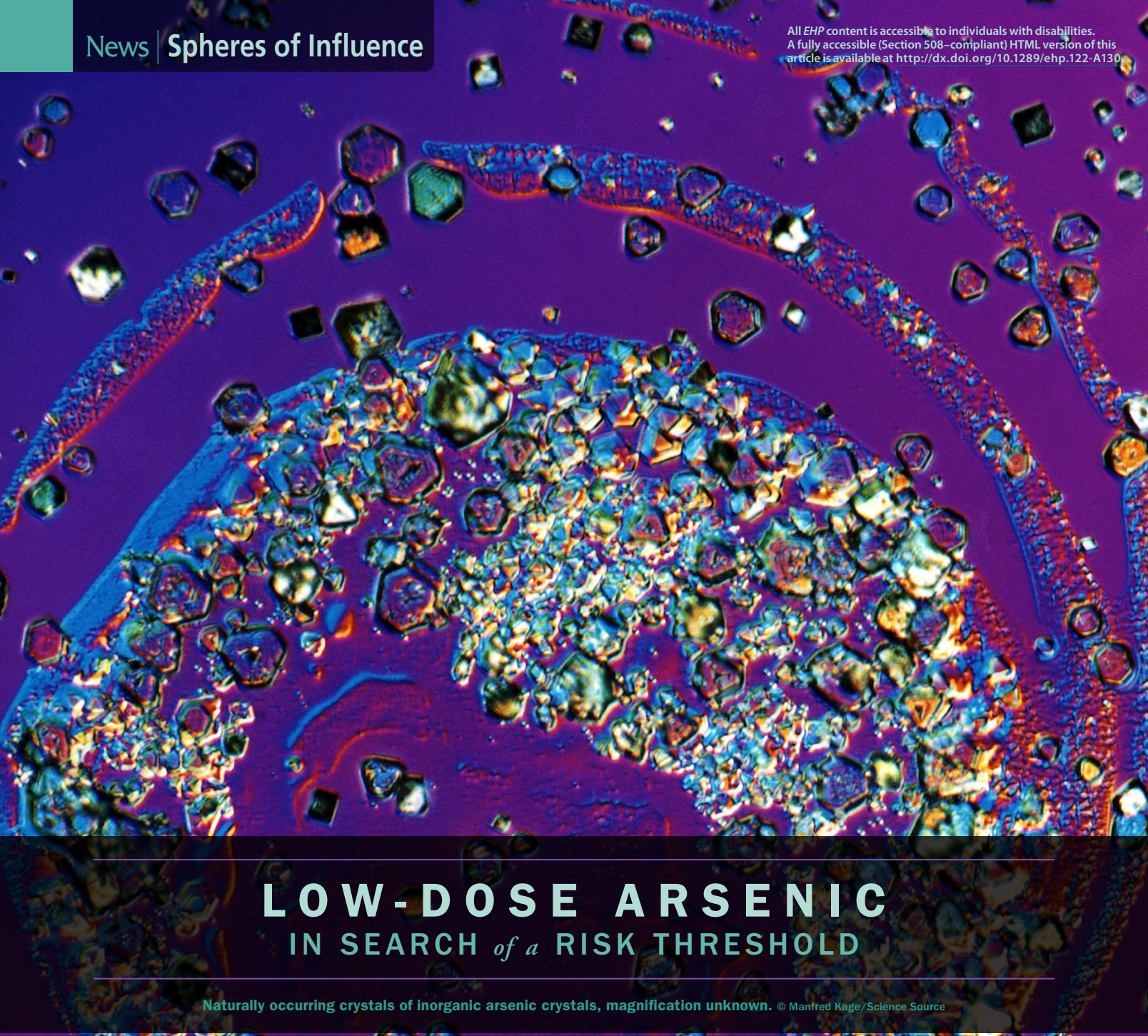

LOW-DOSE ARSENIC
IN SEARCH *of a* RISK THRESHOLD

Naturally occurring crystals of inorganic arsenic crystals, magnification unknown.

Scientists long ago linked high levels of arsenic in groundwater to cancer and other environmental illnesses, particularly in Taiwan, Bangladesh, and South America, where the contamination can often reach extraordinarily high levels of 1,000 ppb or more. Now concerns are shifting to the health effects of much lower doses such as those that many Americans live with every day.

Margaret Karagas, who directs the Children's Environmental Health and Disease Prevention Research Center at Dartmouth College, says researchers increasingly believe that arsenic risks are more widespread than previously recognized, particularly during vulnerable periods such as pregnancy and childhood. Protecting against low-level exposure is challenging, however, given that arsenic is a natural element in the Earth's crust and ubiquitous throughout the environment.

Moreover, the evidence for low-dose effects is controversial. One view holds that arsenic has a dose threshold below which exposures aren't harmful. But controversial studies in the peer-reviewed literature increasingly suggest this threshold may not exist, so that any exposure—no matter how small—could boost risks for diabetes, heart disease, immunological problems, and cancer.[1,2,3,4,5,6]

The disagreement is a problem for regulators who face mounting pressure to set or reduce standards for arsenic. The U.S. Environmental Protection Agency (EPA) is grappling with a revised estimate of arsenic carcinogenicity that, if enacted, would result in unattainable clean-up standards, according to Susan Griffin, a senior toxicologist with the EPA's Region 8 office in Denver, Colorado. The U.S. Food and Drug Administration (FDA) is also under pressure to regulate arsenic in foods, especially rice, which readily absorbs the metal as it grows, making it a top source of dietary exposure.

The focus on rice comes on the heels of a new "action level" of 10 ppb for arsenic in apple juice that was proposed by the FDA in July 2013.[7] This new value, which tightens the agency's previous "level of concern" of 23 ppb (and which has yet to be formally adopted), was motivated in part by mounting publicity over low doses of arsenic in the diet, including media-directed efforts by the public-interest group Consumers Union (CU) to raise awareness on the issue. Growing public scrutiny has put a spotlight on the complex question of how very low arsenic exposures may affect human health.

A Historical View

That arsenic can be lethal has been known since antiquity. But lethal doses of arsenic are difficult to quantify, and they depend on solubility, valence states, and other factors. The Agency for Toxic Substances and Disease Registry suggests that the minimal lethal exposure in humans ranges from 1 to 3 ppm, with death resulting from cardiovascular collapse and hypovolemic shock.[8]

Researchers didn't perceive arsenic as an environmental health threat until studies in Taiwan, and later in Chile, linked levels in groundwater with skin cancers such as squamous cell carcinoma (which is rarely fatal) and a condition called black foot disease (which affects blood vessels, leading to gangrene). Villagers were exposed to the arsenic beginning in the early twentieth century after artesian wells were drilled throughout southwestern Taiwan to avoid saltwater intrusion from shallower wells.[9] The U.S. Public Health Service aimed to protect against the arsenic-related skin problems seen in Taiwan when it set a 50-ppb standard for arsenic in drinking water in 1942, which was then adopted by the EPA in 1975.[10]

The levels deemed "low" in early environmental health research on arsenic were much higher than what's considered low today. Studies from Taiwan up to the 1980s described groundwater levels of up to 300 ppb as low, of up to 600 ppb as moderate, and values beyond that as high.[10,11] These delineations were based on a view that consuming arsenic in groundwater, while harmful, wasn't fatal in the long run.

Two pivotal studies led researchers to reconsider that point. Chien-Jen Chen, who was then a teaching assistant at the National Taiwan University College of Medicine, and colleagues showed that arsenic could, in fact, boost risks for fatal malignancies at groundwater concentrations far less than 600 ppb. Published in 1985, the first study reported statistically significant associations between chronic exposure to artesian well water in Southwestern Taiwan and elevated mortality from cancers of the lung, bladder, and other internal organs.[12,13] And in their follow-up study, Chen and colleagues reported that this relationship was dose-dependent—i.e., that cancer rates grew with higher arsenic exposure—and that mortality rates were especially high in areas where blackfoot disease also was endemic.[11]

Joseph Graziano, a professor of environmental health sciences and pharmacology at Columbia University, says Chen's data had far-reaching consequences that scientists are still grappling with today. Without evidence to the contrary, the EPA defaulted to what is still a standard regulatory assumption: namely that any exposure to a carcinogen, no matter how small, increases cancer risk to some degree. Therefore, the National Research Council (NRC) now describes arsenic levels beyond 150 ppb as high, between 150 ppb and 50 ppb as moderate, and below 50 ppb as low.[14]

But linear assumptions drive considerable risk even at low exposures. Extrapolating from high-dose human data, the NRC predicted in 1999 that the 50-ppb water standard could induce cancer in as many as 1 in 100 people.[15]

Arsenic in U.S. Private Wells

Despite the 10-ppb upper limit on inorganic arsenic in municipal water, neither the EPA nor state governments regulate arsenic in private wells. However, a 2001 EPA study found that 13 million U.S. residents get their drinking water from private wells that exceed the federal arsenic standard.[35,36,37] Similarly, in 2009 the U.S. Geological Survey (USGS) tested 1,774 private wells nationwide and found that 6.8% of them exceeded the EPA standard (these are the most recent national data available on arsenic in private wells).[38]

According to Leslie DeSimone, a water quality specialist with the USGS, 90% of the exceedances were below 50 ppb, but measured concentrations ranged as high as 242 ppb, with the highest levels detected in the West, Midwest, parts of Texas, and New England. During a survey of Maine wells conducted in the mid to late 2000s, USGS scientists measured a concentration of 3,100 ppb in the coastal town of Danforth.[39] Maine resides within a belt of arsenic-laden bedrock that extends north from New York.

Bill Wilber, chief of the USGS National Water Quality Assessment Program, says in some cases simply drilling a well introduces oxygen and other elements that alter the chemistry of the underlying geology, liberating arsenic from bedrock and allowing it to seep into the water column. "So you can find a big exceedance in one well and not in another that's just fifty feet away," Wilber says.

According to Andy Smith, state toxicologist with the Maine Division of Environmental Health, the cost of a home-based system to remove arsenic from well water ranges from $300 for a point-of-use system (i.e., at the faucet) to as much as $9,000 for point-of-entry systems that treat water for the whole household. Federal or state assistance to purchase these systems generally isn't available, Smith says.

By that time, the EPA had already been engaged in technical review on arsenic for years. The agency ultimately evaluated more than 300 studies and drew on expert opinions from the NRC, the National Drinking Water Council, and its own Science Advisory Board (SAB) before it finally dropped the standard from 50 to 10 ppb in 2001[16]—a level the NRC estimated might lead to a cancer risk of approximately 1 in 300 for people exposed over a lifetime.[17] According to Craig Steinmaus, an associate adjunct professor in epidemiology at the University of California, Berkeley, School of Public Health, the EPA by necessity had to factor cost and technical feasibility as well as health into the 10-ppb drinking water standard.

Debating the Standard

The EPA's risk assumptions on arsenic were criticized by researchers who felt it was inappropriate to extrapolate low-dose effects from the high-dose Taiwanese studies. Samuel Cohen, a professor of pathology and microbiology at the University of Nebraska Medical Center, has long maintained that arsenic has a dose threshold below which exposures are not harmful. According to Cohen's own research with rodents (in addition to *in vitro* and *in vivo* studies by other researchers), arsenic is carcinogenic only at doses high enough to induce cytotoxicity followed by regenerative cell proliferation. If prolonged, he says, that mechanism can spawn tumors in the bladder, lungs, and skin.

But Cohen insists this whole process depends on the generation of reactive arsenic metabolites that, in turn, interact with sulfhydryl groups in critical cell proteins. And at minimal doses (below 10 ppb in drinking water given to experimental animals or 100 ppb in well water consumed by humans, he says), arsenic exposure doesn't generate enough reactive metabolites to induce tumor growth, suggesting that arsenic has a dose threshold. Moreover, Cohen claims that only direct reactions with DNA produce linear, nonthreshold dose responses for cancer, but according to the evidence, he says, inorganic arsenic is not DNA-reactive.[18]

"A linear dose–response line goes against what we know about arsenic's basic biology," Cohen says. "What we show in the lab shows there must be a threshold phenomenon."

Other scientists disagree. Steinmaus, for instance, counters that rodents may not be good models for human arsenic metabolism given that "they don't get cancer at doses that clearly cause cancer in humans." He says, "You need to interpret those data cautiously."

Moreover, high-dose human data from Taiwan are valuable because they remove some of the uncertainty associated with

exposure, Steinmaus claims. Villagers in Taiwan often spend much of their lives in one general location, so the arsenic measured in local well water likely reflects their actual long-term intake. By contrast, populations in the United States and other developed countries with lower arsenic levels in groundwater are more mobile, leading to a strong likelihood of exposure misclassification. This statistical bias occurs when individual subjects in epidemiology studies are classified as having consumed more—or less—of a substance over a given duration than they actually ingested, making it difficult to accurately estimate disease associations.

Thus, the EPA SAB concluded in 2010 that—given the size and stability of the population, as well as the inclusion of long-term exposure patterns—the Taiwanese data were "still the most appropriate source for estimating bladder and lung cancer risk to humans."[10] But the SAB also stated that published studies from countries with low levels of arsenic in drinking water (which the SAB defined as up to 160 ppb) should be critically evaluated.[10]

Evidence for Low-Dose Impacts

Low-dose studies are now ongoing in a number of countries, including various locations throughout the United States. For instance, in 2013 Ana Navas-Acien, an associate professor of environmental sciences and epidemiology at the Johns Hopkins Bloomberg School of Public Health, published results from a prospective study showing that urinary arsenic concentrations reflecting low and moderate drinking water exposures were associated with lung, prostate, and pancreatic cancer,[5] as well as with cardiovascular disease,[2] among Native Americans living in Arizona, Oklahoma, and the Dakotas.

Navas-Acien's team measured arsenic in urine samples that had been collected and frozen between 1989 and 1991. The cohort of nearly 4,000 individuals had originally been assembled for the Strong Heart Study (SHS), an evaluation of cardiovascular health in Native Americans launched by the National Heart, Lung and Blood Institute in 1988. According to Navas-Acien, Native Americans included in the SHS tend to be more geographically stable than the general U.S. population, limiting the potential for exposure misclassification.[5] "They get the same exposure to arsenic year after year that they got at birth," she explains.

By matching local well water data collected by the EPA and urinary arsenic measures from the SHS samples with information from death certificates up through 2008, Navas-Acien could study the relationship between arsenic exposure and cancer mortality. Her team's results suggested that arsenic had a linear dose response with lung cancer in particular, although Navas-Acien points out that confidence intervals were wide at doses below 5 ppb in well water, indicating uncertainty at the lowest exposure levels.

A similar linear response was also estimated for prostate and pancreatic cancer, but with even wider confidence intervals at the lowest doses. However, the excess relative risks estimated for prostate and pancreatic cancer in Navas-Acien's study are much greater than they are for lung cancer; this is inconsistent with findings from other areas such as Taiwan, and therefore raises questions among some researchers about the validity of the findings. Navas-Acien's team didn't evaluate bladder cancer or skin cancer because of the small number of cases.

In a separate study of the same SHS cohort, Navas-Acien reported an association between low-dose arsenic exposures and higher rates of cardiovascular disease.[2] That study is one of the first prospective cohort studies to evaluate arsenic-related cardiovascular risk, including both incidence and mortality, in a population from the United States.

These findings add to a wealth of data emerging from what could be the largest evaluation of arsenic toxicity yet undertaken: the Health Effects of Arsenic Longitudinal Study (HEALS), which launched in Bangladesh in 2000.[19] Coordinated by Graziano and Habibul Ahsan, a professor of epidemiology, medicine, and human genetics at the University of Chicago, HEALS has over time assembled a cohort of tens of thousands of individuals living in the district of Araihazar, where arsenic levels measured in well water have ranged from nondetectible to more than 900 ppb.

The HEALS team first reported an association between arsenic and high blood pressure in 2007 at well water concentrations of 10–40 ppb. Since then, HEALS has yielded dozens of papers associating arsenic at levels below 50 ppb with health conditions including heart disease, hematuria (blood in the urine), and impaired lung function.[20,21,22] Studies also showed that increased total urinary arsenic was associated with skin lesions such as melanosis and keratosis, which are known precursors to skin cancer.[23,24] "HEALS is an ongoing effort, and we are expanding the design and questions that we can answer with longer follow-up," Ahsan says.

The Regulatory Landscape

Confronted with mounting evidence of arsenic's low-dose effects, its commercial uses are being phased out. Of particular concern are uses in agriculture, which can result in potentially significant human exposures. According to a November 2013 NRC report, foods dominate human arsenic exposures when the levels in drinking water drop below 50 ppb (drinking water drives the exposures when its arsenic content exceeds that amount).[14]

In some cases, agricultural soils are naturally high in arsenic, but arsenical herbicides also can leave residues that accumulate in crops. Most of these herbicides have now been phased out (with some exceptions made for turfgrass and cotton),[25,26] but what remains in soil from past applications has been especially problematic in apple orchards, where these herbicides were routinely used, and in rice grown on old cotton fields that were treated with the chemicals.

Arsenical feed additives used to promote growth and prevent disease in poultry and swine may also be problematic for human consumers. However, these additives are also being phased out. Production of the feed additive roxarsone ceased voluntarily in 2011 after the FDA detected inorganic arsenic in the livers of chickens that ate it.[27] The manufacturers of roxarsone and two other arsenical feed additives have requested that the FDA withdraw approval of these products.[28] The agency is currently considering a request to ban a fourth additive, nitarsone.[28]

Now the FDA is weighing how to impose standards for arsenic in foods. The proposed standard of 10 ppb in apple juice was a first step in this direction, but advocates with CU say the agency should go further by imposing a 120-ppb standard for inorganic arsenic in rice.[29] In November 2012 CU published the results of a study showing that 223 samples of rice and rice-based products sold in the United States contained inorganic arsenic at concentrations ranging from 29.4 to 210 ppb.[30] In addition, Dartmouth investigators reported that brown rice syrup, a sweetener, might expose consumers to "significant concentrations" of inorganic arsenic.[31] (Arsenic tends to accumulate in the aleurone layer of the rice grain, which gives brown rice its color. This layer is removed to produce white rice.[31])

The FDA followed up with its own report on 1,300 samples of rice and rice products, which found that concentrations of inorganic arsenic ranged from an average 0.1 µg per serving in infant formula to an average 7.2 µg per serving in brown rice.[32] For perspective, Aaron Barchowsky, a professor of environmental and occupational health at the University of Pittsburgh School of Public Health, says that daily consumption of 3 liters of water at the 10-ppb standard amounts to a 30-µg dose of inorganic arsenic.

In a 6 September 2013 statement, the FDA said the amount of detectable arsenic in the sampled rice and rice products was too low to cause "any immediate or short-term adverse health effects."[33] FDA spokesperson Shelly Burgess says the statement referred to short-term effects only, and not skin, bladder, or lung cancer.

But Michael Crupain, director of *Consumer Reports*' Food Safety and Sustainability Center, insists that chronic low-level exposures over time are still a concern, especially for infants fed formula made with brown rice syrup, which had the highest levels detected in CU's survey. The FDA is now performing a draft risk assessment for arsenic in rice, which agency officials say could guide further actions.

Also on the regulatory front, the EPA is grappling with its numerical estimate of arsenic's cancer potency. This value, known as a cancer slope factor (CSF), guides important regulatory policies, including clean-up standards at contaminated waste sites. Set in 1998, the original CSF for arsenic was based on nonmelanoma skin cancers observed in the early Taiwanese studies.

In 2010 the EPA proposed a revised CSF as part of an arsenic reassessment under the agency's Integrated Risk Information System (IRIS).[10] The proposed CSF, which was based on newer reports of associations with more dangerous lung and bladder cancers, was 17 times greater than the older value. But that new value was protested by industry and other affected stakeholders, even some of the agency's own scientists. Griffin, of EPA Region 8, says that with the revised CSF, arsenic clean-up levels would drop 100-fold, which is below natural background levels of arsenic in western states.

The proposal was subsequently dropped by the EPA, and under a congressional mandate the agency is now revising its arsenic reassessment with a focus on both cancer and noncancer end points. On 7 November 2013 the NRC presented a report that the EPA will use for guidance in drafting a new IRIS document.[14] Graziano, who chairs the NRC committee, says the EPA will submit the revised document by 2015. And at that point, he says, NRC scientists will review it to ensure that dose–response relationships between inorganic arsenic and its effects are "appropriately estimated and characterized."

Continued Debate

Meanwhile the debate over low-dose health risks from arsenic will likely continue on two fronts: how to apply mechanistic findings from animal and *in vitro* research to human responses, and how to address fundamental uncertainties in the human data.

A key question is whether the recent epidemiological literature supports estimates of cancer risk predicted from linear dose–response models. Dozens of studies over the last 15 years have investigated human cancer risk from arsenic exposure at sites around the world. According to a 2011 review published by Herman Gibb, president of environmental consulting firm Tetra Tech Sciences, these studies provide conflicting evidence, in part because the sample sizes needed to quantify risks at drinking water doses less than 100 ppb are larger than what's ordinarily achievable.[34]

Steinmaus argues that the high-dose epidemiology data may ultimately be most suitable for risk assessment, "but when you extrapolate down from those doses, the risks are huge." He adds, "This raises the question of whether linear extrapolations are suitable, and herein lies the big controversy."

Charles W. Schmidt, MS, an award-winning science writer from Portland, ME, has written for *Discover Magazine*, *Science*, and *Nature Medicine*.

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Arsenic and cancer: evidence and mechanisms

Rachel M. Speer[1], **Xixi Zhou**[1], **Lindsay B. Volk**[1], **Ke Jian Liu**[1,2,*], **Laurie G. Hudson**[1]

[1]Department of Pharmaceutical Sciences, College of Pharmacy, University of New Mexico, Albuquerque, New Mexico, USA

[2]Stony Brook Cancer Center, Renaissance School of Medicine, State University of New York Stony Brook, Stony Brook, NY 11794, USA

Abstract

Arsenic is a potent carcinogen and poses a significant health concern worldwide. Exposure occurs through ingestion of drinking water and contaminated foods and through inhalation due to pollution. Epidemiological evidence shows arsenic induces cancers of the skin, lung, liver, and bladder among other tissues. While studies in animal and cell culture models support arsenic as a carcinogen, the mechanisms of arsenic carcinogenesis are not fully understood. Arsenic carcinogenesis is a complex process due its ability to be metabolized and because of the many cellular pathways it targets in the cell. Arsenic metabolism and the multiple forms of arsenic play distinct roles in its toxicity and contribute differently to carcinogenic endpoints, and thus must be considered. Arsenic generates reactive oxygen species increasing oxidative stress and damaging DNA and other macromolecules. Concurrently, arsenic inhibits DNA repair, modifies epigenetic regulation of gene expression, and targets protein function due its ability to replace zinc in select proteins. While these mechanisms contribute to arsenic carcinogenesis, there remain significant gaps in understanding the complex nature of arsenic cancers. In the future improving models available for arsenic cancer research and the use of arsenic induced human tumors will bridge some of these gaps in understanding arsenic driven cancers.

Keywords

arsenic; cancer; carcinogenesis; DNA damage; mechanism

INTRODUCTION

Over millennia, humans have harnessed the unique properties of arsenic for medicinal, agricultural, commercial, and decorative purposes. At the same time, humans have been subject to the stealthy toxicity of arsenic as an odorless and tasteless, intentional or unintentional, poison. Our complicated relationship with arsenic continues to this day.

Therapeutic uses of arsenic have been documented for thousands of years in traditional Chinese medicine and early western medicine. Two forms of arsenic were included in the

*Corresponding author: kliu@salud.unm.edu.

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Shennong Materia Medica in 200 BCE and Hippocrates is believed to use arsenic pastes to treat skin disorders (Au, 2011; Hughes et al., 2011; Paul et al., 2022; Chen & Costa, 2021). In 1786 Thomas Fowler reported on the medicinal effects of his arsenic solution for a broad range of infectious diseases and skin and blood disorders, in addition to other health conditions. The noted antimicrobial properties of arsenic led to the development of Salvarsan in the early 1900s as an effective treatment of syphilis garnering a Nobel prize for Paul Ehrlich in 1908. In the past, various forms of arsenic, including those used in traditional Chinese medicine and Fowler's solution, were employed as cancer therapeutics especially for cancers of the blood and skin (Au, 2011; Hughes et al., 2011; Paul et al., 2022; Chen & Costa, 2021). The FDA approved arsenic trioxide as a chemotherapeutic for leukemia in 2000 bringing an ancient drug into the modern era.

Other arsenic compounds have been beneficial as rodenticides, pesticides for agricultural crops and wood preservatives (Hughes et al., 2011; Bencko and Foong, 2017). Arsenic-based pigments were used in paints, fabrics and wallpapers based on a coveted emerald green color (Hughes et al., 2011). However, the medicinal and non-medicinal uses of arsenic revealed human toxicities based on unintended exposures. Widespread use of lead arsenate as a pesticide in apple and cherry orchards ultimately led to an official ban in the United States in 1988 (Hughes et al., 2011). The lasting legacy of this use is evident in millions of acres of land contaminated with lead arsenate. Chromated copper arsenate continues to be used as a wood preservative for non-residential purposes and organic arsenicals remain in restricted use as broad-spectrum herbicides. The potential for further contamination of soils and water by inorganic and organic arsenic compounds is under periodic review by the US Environmental Protection Agency (EPA).

Arsenic toxicity has been exploited for political gains through strategic poisonings leading to the often quoted statement labeling arsenic as the "king of poisons and poison of kings". Modern toxicological focus largely centers on the human health consequences of medicinal, occupational and environmental exposures to arsenic. Studies on health effects of human exposures through natural or anthropogenic arsenic contamination in soils and water led to adoption of drinking water standards worldwide currently at 10 ppb. Despite efforts to limit arsenic exposures, it is estimated that 200 million people or more are exposed to toxic levels of arsenic worldwide (Costa 2021). This chapter will focus on arsenic carcinogenicity and cover human population evidence for arsenic as a carcinogen, mechanisms of arsenic carcinogenicity, the carcinogenic potential of different forms of arsenic and conclude with a brief discussion of areas for future research.

SECTION 1: HUMAN STUDIES

Arsenic is a worldwide health concern due to prevalence in the environment and established human toxicity (Podgorski, 2020; Agency for Toxic Substances and Disease Registry (ATSDR), 2007; ATSDR, 2016; Naujokas et al., 2013). Arsenic is present in rocks, soil and water, and background environmental levels may be increased by mining, burning of fossil fuels, and application of agricultural pesticides and herbicides (Gundert-Remy et al., 2015). In recognition of its toxic potential, arsenic is at the top of the ASTDR Priority List (https://www.atsdr.cdc.gov/spl/index.html). Occupational exposures are limited by the US

Occupational Safety and Health Administration to 10 μg/m^3, and recommended drinking water exposure limits of 10 μg/L (10 ppb) have been established by the EPA and the World Health Organization (WHO) (WHO, 2011; EPA, 2014).

The majority of human population studies focus on chronic arsenic ingestion through drinking water as the predominant exposure route (Andrew et al., 2003; Banerjee et al., 2007; Podgorski, 2020, ATSDR, 2007, ATSDR, 2016; WHO, 2011). Many parts of the world have high levels of arsenic in groundwater and aquifers with populations that use these water sources for household needs. One arsenic prediction model based on household groundwater-usage statistics estimates that between 94 and 220 million people may be exposed to high arsenic concentrations (Podgorski, 2020). Indeed, many seminal health studies have focused on populations in areas of the world with high levels of arsenic in water sources including, but not limited to, Bangladesh, India, Taiwan and Chile (ATSDR, 2007; ATSDR, 2016; Banerjee et al., 2017; Farzan et al., 2021; Moore et al., 2002). Some studies have established the relationship between arsenic levels in water and arsenic in biological specimens such as urine, hair and nails (Mahata et al., 2003; Maki-Paakkanen et al., 1998; Ruíz-Vera et al., 2019).

More recently, greater attention has been paid to food as a source of arsenic exposure (Oberoi 2014; Gundert-Remy 2015; Arslan et al., 2017; Wong et al., 2022). Food crops may contain elevated arsenic levels through irrigation with arsenic-containing water, cultivation in arsenic contaminated fields, or use of agricultural products containing arsenic (Gundert-Remy et al., 2015; Wong et al., 2022). Rice has become a notable concern due to arsenic's uptake and accumulation in this plant compared to other common grains such as wheat (Karagas et al., 2019). There is evidence of greater urinary arsenic in individuals reporting higher rice consumption compared to those with low rice consumption even in areas of low arsenic drinking water exposure (Gossai et al., 2017).

The relationships between arsenic exposure and cancer are clear. Cancer is one of the health effects of concern; arsenic is classified as a Class I human carcinogen by the International Agency for Research on Cancer (IARC) with strong experimental and human population evidence to support arsenic carcinogenicity (IARC, 2004; Moore et al., 2002; Srinivas et al., 2019; Tam et al., 2020). The strongest evidence for organ-specific arsenic carcinogenicity is in skin, lung, bladder and kidney with evidence for arsenic contributions to other cancers (WHO, ATSDR, 2007, ATSDR, 2016; Palma-Lara et al., 2020) (Figure 1).

Skin Cancer

Various non-cancerous skin lesions are associated with long term exposure to inorganic arsenic including changes in pigmentation, plantar-palmar hyperkeratinization and hyperkeratotic warts and corns (ASTDR, 2007; Hunt et al., 2014). These skin changes are most common in areas with high arsenic levels in drinking water and are viewed as sensitive indicators of chronic arsenic exposure (ASTDR, 2007; Hunt et al., 2014; Cheng et al., 2016). Skin lesions and cancer appear to be more prevalent at exposures to drinking water levels in excess of 50 μg/L and evidence linking arsenic to skin cancer is less conclusive at lower arsenic levels (Boffetta et al., 2020, Lamm et al., 2021; Karagas et al., 2015). Recent

findings suggest that ingestion of arsenic containing foods in the diet such as rice may also contribute to skin cancer risk (Karagas et al., 2019; Gossai et al., 2017).

The most common tumors associated with arsenic exposure are keratinocytic tumors including squamous cell carcinomas, which may develop from hyperkeratotic warts or corns, and basal cell carcinomas (ASTDR, 2007; Karagas et al., 2015; Palma-Lara et al., 2020). There is less consistent evidence for arsenic-associated melanoma although it has been reported in Bangladesh (Choudhury et al., 2018), but not in the United States (Langston et al., 2022; Bedaiwi et al., 2021; Yager et al., 2016) or there are too few studies to draw firm conclusions (Matthews et al., 2019).

Lung Cancer

Epidemiological evidence indicates increased incidence of lung cancer in workers exposed to arsenic in the copper mining and smelting industry and ingestion through contaminated water (ASTDR 2007; Smith et al., 2012; Steinmaus et al., 2014; Palma-Lara et al., 2020). Studies conducted in Chilean cohorts born during periods of low versus high arsenic exposure from water reveal increased incidence of several cancers, including lung cancer, associated with the high exposure period (ASTDR, 2010; Smith et al., 2006). Similarly, mitigation efforts to decrease arsenic ingestion from contaminated water in Taiwan led to reduction in lung cancer rates (Su et al., 2011). No associations were identified for lung cancer and arsenic in soil in Taiwan despite reported associations between lung cancer and other metals in the same soils (Huang et al., 2013). These findings and others support the conclusion that lung cancer is increased upon chronic exposure to arsenic in drinking water (ASTDR, 2007; Kuo et al., 2017a; Su et al., 2011; Chen et al., 2010; Heck et al., 2009). There is evidence for dose dependence (Chen et al., 2010); however, the associations are less strong at low arsenic exposures (Shao et al., 2021; Tsuij et al., 2019)

The most common type of lung cancer associated with arsenic exposure is squamous cell carcinoma (Kuo et al., 2017; Heck et al., 2009; Taeger et al., 2009). The correlation between arsenic and squamous cell carcinoma was more pronounced at higher exposure levels; adenocarcinoma and small cell carcinoma of the lung were not associated with arsenic level in the drinking water in a Taiwan population (Kuo et al., 2017) although other investigators reported increased adenocarcinoma and small cell carcinomas of the lung with arsenic exposure (Chen et al., 2010; Guo et al., 2004). A study of former German uranium miners exposed to arsenic found that the arsenic-related type of lung cancer differed in miners based on evidence of silicosis. Arsenic was associated with increased squamous cell carcinoma in miners without silicosis. In contrast non-small cell lung cancer was related to arsenic exposure in miners with silicosis (Taeger et al., 2009) suggesting that other underlying factors may influence the specific lung cancer arising because of arsenic exposure.

Bladder Cancer

Population studies identify a clear relationship between elevated arsenic levels in drinking water and bladder cancer (IARC, 2004; ASTDR, 2007; Smith et al., 2012; Krajewski et al., 2021). A recent study found evidence for oxidative DNA damage in residents exposed to arsenic from artesian well-water in Taiwan and concluded that arsenic exposure and

DNA damage predicted the risk of bladder cancer (Tsai et al., 2021). In the US, arsenic concentrations in drinking water were positively associated with bladder cancer in both men and women (Mendez et al., 2017; Baris et al., 2016) and a spatial cluster analysis of bladder cancer mortality identified significant hot spots. Further study concluded that there was a significant association between bladder cancer mortality and arsenic intake from well water (Amin et al., 2019; Baris et al., 2016). Notably, well water is not subject to federal regulation and may exceed the EPA recommended maximum contaminant level. As with other arsenic-associated cancers, there is not uniform agreement on risks linked to lower exposures (Kayajanian, 2003) although a meta-analysis suggested that exposure to 10 μg/L of arsenic in drinking water may double the risk of bladder cancer (Saint-Jacques et al., 2014). Arsenic ingestion through food is also considered a potentially important source of exposure that may contribute to bladder and other cancers (Gundert-Remy et al., 2015; Oberoi et al., 2014; Karagas et al., 2019).

There are several studies that indicate arsenic exposure may influence bladder cancer progression and clinical outcomes. Comparisons of clinicopathological characteristics in bladder cancer patients from an arsenic contaminated region versus two reference areas found significantly greater proportions of locally advanced and high-grade tumors in the arsenic-exposed patients (Fernandez et al., 2020). Patients from areas of high arsenic exposure in Taiwan versus low arsenic exposure found worse prognosis in the patients from areas of high arsenic and this was most pronounced in the disease-free survival of early-stage disease (Chang et al., 2021). Similar findings were reported for patients in West Bengal, India where measured arsenic accumulation in bladder tumor tissue was associated with advanced tumors, poor prognosis and disease recurrence after treatment (Ghosh et al., 2021). These observations may be related to distinct mechanisms of arsenic carcinogenesis (Zhou et al., 2021; Palma-Lara et al., 2020) as described in Section 2.

Additional Cancers and Cancer Risk Due to Prenatal and Early Life Exposure

Although the evidence for arsenic-associated cancers is strongest for skin, lung and bladder tumors, there are other cancers that are linked to arsenic exposure. There is significant evidence for arsenic induced kidney cancer (Smith et al., 2012; Krajewski et al., 2021; Saint-Jacques et al., 2014; Ferreccio et al., 2013a; Naujokas et al., 2013; Palma-Lara et al., 2020; Chen and Costa, 2021) and liver cancer (Naujokas et al., 2013; Palma-Lara et al., 2020; Chen & Costa, 2021; ASTDR, 2010). There is more limited evidence for increased gastrointestinal tract (Krajewski et al., 2021; ASTDR, 2010), laryngeal (Smith et al., 2012), prostate (Lamm et al., 2021) and breast cancer (Moslehi et al., 2020) risk with elevated arsenic exposure (Abuawad et al., 2021). In the case of breast cancer, it appears that genetic factors may play an important modifying role in arsenic-associated risk (Moslehi et al., 2020).

Gestational and early life exposure to arsenic is associated with a variety of long-term health effects including increased risk of cancer in humans (Smeester and Fry, 2018; Martinez and Lam, 2021). Studies conducted in Northern Chile provide strong evidence for the cancer consequences of prenatal and early life arsenic exposures. In 1958, the levels of arsenic in drinking water increased nearly 10-fold to 870 ppb and remediation efforts in the 1970s

reduced arsenic in drinking water to near pre-1958 levels. This led to human cohorts with different levels and timing of arsenic exposure (Smith et al., 2012). Increased mortality rates were observed for bladder, laryngeal, lung, kidney, liver and other cancers (Smith et al., 2012; Ferreccio et al., 2013b; Steinmaus et al., 2014). Long latency patterns of 25 years or more after early life exposure have been reported for liver, kidney and bladder cancers, often accompanied by evidence for higher incidence and cancer mortality in children and young adults (Yuan et al., 2010; Marshall et al., 2007; Liaw et al., 2008). These findings point to arsenic cancer risks that can persist decades after exposure in early life stages. Given evidence from experimental animal models that prenatal arsenic exposure elevates cancer development (Martinez and Lam, 2021; Waalkes et al., 2007), arsenic exposures across the entire lifespan are a concern.

Modifying Factors of Arsenic Carcinogenesis

Arsenic is one of a limited number of metals or metalloids that is metabolized to methylated forms (Roy et al., 2020). Biotransformation of inorganic arsenic to mono and dimethyl forms (MMA and DMA, respectively) occurs through the enzyme arsenic methyltransferase (AS3MT) and arsenic is excreted as a mixture of inorganic and methylated forms (Roy et al., 2020, see also Section 3). Population studies suggest that the different forms of arsenic are not equivalent in carcinogenic potential. Studies of the proportion of inorganic and methylated arsenic species found that individuals with high urinary inorganic percent or low DMA present were more likely to develop bladder cancer (Chung et al., 2013) and a meta-analysis found that bladder and lung cancer were increased significantly with increasing MMA percent in the urine (Melak et al., 2014). Positive associations between percent urinary MMA and cancers of the breast and skin in addition to lung and bladder also have been reported (Abuawad 2021; Gamboa-Loira et al., 2017; Huang et al., 2018). There is increasing evidence that polymorphisms and expression levels of AS3MT may lead to differences in arsenic metabolism (Delgado et al., 2021) and are important factors in arsenic-related cancer risk and outcomes (Song et al., 2020; Huang et al., 2018; Lin et al., 2018; De la Rosa et al., 2017).

Co-exposures of arsenic and DNA damaging agents can amplify carcinogenesis with the greatest evidence in human populations for skin, lung and bladder cancers. The risk of arsenic-associated skin lesions that can be precursors to cancer was greater with sun exposure (Chen et al., 2006). Furthermore, arsenic exposure and smoking increase risk of lung and bladder cancers with evidence for significant arsenic dose effect (Tsuda et al., 1995; Karagas et al., 2004; Chen et al., 2010; Chen et al., 2004; Koutros et al., 2018; Ferreccio et al., 2013b). These population-based findings are consistent with experimental findings of arsenic co-carcinogenesis (Zhou et al., 2021). Cumulatively, the evidence derived from studies of human populations exposed to arsenic indicate that arsenic is a human carcinogen both as a single agent and the carcinogenic effects can be modified by multiple factors including genetic polymorphisms and toxic co-exposures.

SECTION 2: MECHANISMS OF ARSENIC CARCINOGENESIS

The diverse range of cellular effects of arsenic exposure create a complex landscape for studying arsenic carcinogenesis. Many processes affected by arsenic exposure are interconnected further complicating our understanding of arsenic's effects. This section will discuss key mechanisms of arsenic carcinogenesis focusing on oxidative stress, the role of DNA damage and repair in genotoxicity, epigenetic changes, and how arsenic interacts with proteins to affect major pathways of carcinogenesis.

Oxidative Stress

Oxidative stress is a cornerstone of arsenic toxicity and carcinogenesis. It plays a role in DNA damage, repair inhibition and cellular mechanisms related to cell stress and cell death. Arsenic induces elevated levels of reactive oxygen species (ROS) and reactive nitrogen species (RNS) that are damaging to macromolecules in the cell including DNA and protein (Ding et al., 2005; Wang et al., 2013) (Figure 2). Oxidative stress due to arsenic exposure is initiated by intracellular metabolism of arsenic, which involves glutathione (GSH) as a necessary mediator. GSH depletion during arsenic metabolism may result in reduced ability to ameliorate damaging ROS, both endogenous and those produced by the direct effects of arsenic in the cell. Arsenic metabolism also produces additional reactive intermediates. For example, the dimethylarsenic peroxyl radical, which is formed in the metabolism of dimethylarsenic acid, a methylated form of inorganic arsenic, further requires antioxidant remediation, and this intermediate has been shown to induce DNA damage (Flora et al., 2007; Yamanaka, 1994; Yamanaka et al., 1995). Specific forms of arsenic and their effects on oxidative stress are discussed in Section 3.

In general, reactive species arise due to the reduction of molecular oxygen to form superoxide radical anions ($O_2^{\cdot -}$), hydrogen peroxide (H_2O_2), hydroxyl radicals (•OH), hydroperoxyl radicals (HOO•), singlet oxygen (O_2), and peroxyl radicals (ROO•) (Wiseman and Halliwell, 1996). Arsenic facilitates the formation of these species by targeting several different processes. The role of arsenic in production of ROS is observed in the mitochondria where it causes dysregulation of the electron transport chain (Hosseini et al., 2013). Arsenic inhibits succinate dehydrogenase activity responsible and altering the balance of oxidative phosphorylation and O_2 production which perpetuates formation of additional ROS while also altering mitochondrial membrane potential (Hosseini et al., 2013; Yen et al., 2012). Mitochondria also contain elevated levels of sulfhydryl containing enzymes due to their redox-prominent role making many enzymes in the mitochondria molecular targets of arsenic exposure (Netto et al., 2002). Arsenic induced ROS also leads to formation of oxidative DNA damage, which can be measured as 8-hydroxy-2'-deoxyguanosine (8-OHdG) (Chayapong et al., 2017; Ding et al., 2005; Kessel et al., 2002). NADPH oxidase (NOX), which is activated by arsenic and stimulates increased generation of ROS, is one mechanism of increase DNA damage through oxidative stress (Cooper et al., 2022).

Arsenic causes various forms of cellular damage, which enhances the formation of radicals in the cell, adding to oxidative stress. For example, arsenic exposure leads to the formation of oxidized lipids, which can be used as a biomarker for arsenic-induced oxidative

stress. Lipid peroxidation contributes to protein damage and compromised mitochondrial permeability forming a cycle of increased damage to macromolecules and ROS (Li et al., 2020; Mahajan et al., 2018; Nutt et al., 2005).

Arsenic generates RNS including nitric oxide (NO•), which further interacts with another product of arsenic exposure, $O_2^{\cdot -}$, to produce peroxynitrite ($ONOO^-$), which can affect DNA and proteins (Pace et al., 2017). $ONOO^-$ induces the nitration of tyrosine in proteins potentially altering their function. $ONOO^-$ also can cause S-nitrosation of cysteine residues in proteins, which was demonstrated in a study on the DNA repair protein, PARP-1 and was inhibited by the production of ROS and RNS after exposure to arsenic (Zhou et al., 2019). Additionally, $ONOO^-$ interacts with guanine forming 8-nitroguanine, which is used as a biomarker for RNS production (Kawanishi and Hiraku, 2006). Levels of arsenic exposure have been correlated with increased levels of 8-nitroguanine in epidemiology studies (Navasumrit et al., 2019; Phookphen et al., 2017). Arsenic-induced ROS and RNS increase oxidative stress leading to direct and indirect damage to DNA, proteins, and signaling pathways involved in maintaining genomic integrity. These effects are further discussed in the following sections.

Genotoxicity

Arsenic carcinogenesis is a complex process. However, the current body of research suggests genotoxicity arising as damage to genetic information is a key driver of arsenic-induced cancers and is a result of combined induction of DNA damage, inhibited DNA repair, and aberrant cell division. Genotoxicity begins with damage to genetic material. There is sufficient data showing arsenic exposure results in various forms of DNA damage including DNA double- and single-strand breaks and other lesions such as 8-nitroguanine and 8-OHdG as discussed above (Ding et al., 2005; Dong and Luo, 1993; Dutta et al., 2015; Okayasu et al., 2003). However, arsenic does not directly interact with DNA to cause damage, and there is a lack of strong evidence of arsenic forming adducts with DNA. Instead, studies show arsenic induced oxidative stress is responsible for the majority of DNA damage after arsenic exposure (Kumar et al., 2016). Studies show RNS and ROS inhibitors and pre-treatment with antioxidants attenuate DNA damage after arsenic exposure suggesting oxidative stress is a major contributor in arsenic-induced DNA damage (Ding et al., 2005; Lynn et al., 1998; Nesnow et al., 2002). This effect was also observed in arsenic-exposed human populations (Biswas et al., 2010) and animal studies (Balakumar et al., 2012; Kadirvel et al., 2007)

DNA double strand breaks are a particularly lethal form of DNA damage and if left unrepaired result in cell death. Arsenic-induced DNA double strand breaks have been identified in a number of studies (Guillamet et al., 2004; Mouron et al., 2006; Okayasu et al., 2003; Xie et al., 2014). If mis-repaired, these DNA double strand breaks in sites of key tumor suppressor genes may lead to changes to the genetic material and carcinogenesis. This result is also true of single-strand breaks and the formation of intra-DNA adducts and crosslinks with proteins and other cellular molecules (Bau et al., 2002; Dong et al., 1993; Mouron et al., 2001; Wang et al., 2001). DNA adducts and DNA-protein adducts may also contribute to the formation of DNA double strand breaks if mis-repaired (Bau et al., 2002, Wang et al., 2001). Several studies show arsenic exposure results in crosslinking of

proteins, including DNA repair proteins, with DNA potentially inhibiting repair processes and contributing to genomic instability (Garman et al., 1997; Gebel et al., 1998; Mustra et al., 2007). In another study arsenic-induced DNA-protein crosslinks were observed with gross chromosomal changes including sister chromatid exchanges, a hallmark of genomic instability (Mouron et al., 2005).

Genomic instability is a common driver of cancers and is associated with exposure to many metals including arsenic (Mitkovska et al., 2020; Wu et al., 2019; Wise and Wise, 2012). DNA damage and dysregulation of cell division induced by arsenic ultimately leads to gross changes to genetic material including formation of micronuclei (Basu et al., 2004; Navasumrit et al., 2019), both numerical and structural chromosome instability (States, 2015), and microsatellite instability (Wu et al., 2017). Numerical chromosome instability associated with arsenic exposure has been observed in both human populations (Dulout et al., 1996), cell culture models (Eguchi et al., 1997; Salazar et al., 2010; Sciandrello et al., 2002), and animal studies (Kashiwada et al., 1998). Numerical chromosome instability can arise due to uncoupling mechanisms involved in cell division, such as changes in mitotic checkpoints and centrosome dysregulation, and is considered a driving force of carcinogenesis (Sansregret and Swanton, 2017). Arsenic induces prolonged mitotic arrest resulting in aneuploidy (Eguchi et al., 1997; Yih et al., 1997). Other studies have shown arsenic disrupts centrosome function (States et al., 2002; Suzuki et al., 2009), which can be carried down through cell populations even after removal of arsenic suggesting these changes may be permanent and heritable (Sciandrello et al., 2002). Another endpoint of altered cell division is the formation of micronuclei, which form as a result of lagging chromosomes and chromosome fragments, and these events have been observed in arsenic-exposed cells (Moore et al., 1996), workers (Lewińska et al., 2007; Vuyyuri et al., 2006), and in populations exposed to arsenic in drinking water (Tian et al., 2001; Warner et al., 1994).

Structural chromosomal changes including chromatid exchanges, ring structures, and dicentric chromosomes have been identified in arsenic-exposed human populations (Banerjee et al., 2007; Ghosh et al., 2006; Mahata et al., 2003). Other studies have identified chromatid gaps associated with arsenic exposure and urine levels (Maki-Paakkanen et al., 1998). Importantly for carcinogenesis, increases in chromosomal aberrations have been associated with arsenic-induced cancers and pre-cancerous lesions. For example, chromosome aberrations were found in patients with arsenic-induced Bowen’s disease (Ghosh et al., 2007), arsenic-induced stomach cancer (Boffetta et al., 2007), and were higher in bladder cancer patients with arsenic exposure than those without (Moore et al., 2002).

Telomere maintenance and stability is closely tied to maintaining genomic stability. Several recent studies in an arsenic exposed human population found exposure was associated with altered telomere length, which is also attributed to enhanced chromosomal instability and cancer (Chatterjee et al., 2018; Villarreal et al., 2019). Guanine bases are a target of arsenic-induced oxidative damage. Thus, telomeres, rich in guanine, are a target of arsenic exposure. For example, Coluzzie et al., 2014 showed telomeric changes, included enriched DNA damage and shortening, occurred because of arsenic-induced oxidative stress. These telomeric changes may contribute to compromised protection provided by telomeres in

maintaining chromosomal integrity. Other studies have identified arsenic-induced oxidative stress as a source of telomere attrition and structural chromosome instability arising as end-to-end fusions, and these effects were reduced by the addition of antioxidants (Liu et al., 2003). Epidemiology studies have confirmed arsenic exposure is associated with decreased telomere length and increased risk of skin carcinomas (Farzan et al., 2021; Grau-Perez et al., 2019; Srinivas et al., 2019) while other studies have shown the opposite (Gao et al., 2015).

The literature supports genomic instability represented as structural and numerical chromosome instability and alterations to chromosome maintenance (telomeres) as a prominent mechanism of arsenic-induced carcinogenesis. While these changes are evident the mechanisms of how they arise are important in understanding arsenic carcinogenesis. Changes in cell division were discussed above in association with numerical chromosome instability. However, structural chromosome instability is most associated with DNA damage (discussed above) and failure of robust DNA repair pathways as discussed below.

DNA repair

Arsenic induces a variety of DNA lesions, each with distinct repair pathways (Figure 3). Inhibited DNA repair after arsenic exposure is considered a driving mechanism of genomic instability and arsenic-induced cancers and research in this area has uncovered detailed cellular mechanisms of arsenic carcinogenesis. Mechanistic studies show arsenic affects critical repair factors in pathways of DNA repair including excision repair pathways, nucleotide excision repair (NER), base excision repair (BER) and strand break repair pathways, homologous recombination (HR), and non-homologous end joining (NHEJ).

Excision repair mechanisms are used to remove oxidative damage to nucleotides. Non-bulky damage to DNA bases, such as arsenic-induced 8-oxoguanine and apurinic and apyrimidinic sites, are repaired by BER. BER has been shown to be essential in repairing oxidative damage after arsenic exposure (Lai et al., 2011). Meanwhile BER genes were found to have decreased expression in HaCaT cells exposed to arsenic exposure (Ding et al., 2021). Specifically, human 8-oxoguanine DNA glycosylase I (Ebert et al., 2011), DNA polymerase β, and APE1 (Sykora and Snow, 2008) were found to have suppressed or altered expression and activity in human lung cells after arsenic exposure contributing to repressed BER function.

NER is responsible for repairing bulky type DNA lesions and is particularly important when considering arsenic as a co-carcinogen. NER repairs bulky lesions such as cyclobutane DNA photoproducts induced by ultraviolet radiation (UVR) and DNA adducts as a result of polyaromatic hydrocarbon (PAH) exposure. Arsenic alters NER through several mechanism. Individuals exposed to arsenic in drinking water were found to have decreased expression of DNA repair genes across in cell culture and human populations (Andrew et al., 2003; Andrew et al., 2006). Studies focused on NER after arsenic exposure have identified specific protein targets of arsenic including XPC, XPA, and ERCC1 (Holcomb et al., 2017; Huestis et al., 2016; Muenyi et al., 2011; Nollen et al., 2009; Zhou et al., 2014). Other mechanisms of arsenic-inhibited NER include inhibited protein function. Arsenic inhibits the activity of DNA ligase III and DNA ligase I (Hu et al., 1998). Extensive studies have also found zinc finger proteins in the NER pathway, including XPA are targeted by arsenic exposure altering

their function and are further discussed in Section 3 below (Huestis et al., 2016; Zhou et al., 2014). In addition to direct protein effects, polymorphisms in NER genes were found to be associated with non-melanoma skin cancer and arsenic exposure (Applebaum et al., 2007).

If NER or BER fail to repair DNA damage, double strand breaks can arise. These breaks are repaired by NHEJ or HR as a final attempt to repair the damage and maintain genomic integrity. However, studies show that both NHEJ and HR are impaired by arsenic exposure. Notably Morales et al., 2016 found arsenic shifted repair to the more error-prone alt-NHEJ pathway from the high-fidelity HR repair pathway potentially resulting in mis-repaired DNA double strand breaks and increased genomic instability. Arsenic has been shown to affect HR repair by altering recruitment of HR repair factors including BRCA1 and RAD51 (Zhang et al., 2014). Arsenic increased sumoylation of Mus18, an endonuclease involved in cyclobutane pyrimidine dimers (CPDs) and 6,4'PP HR repair, resulting in compromised DNA damage response (Hu et al., 2017). PARP-1 may play a role in double strand break repair due to changes to PARylation and therefore recruitment of DNA double strand break repair factors. PARP-1 also plays a role in BER, NHEJ, single strand break repair, and as a zinc finger protein has been shown to be a primary target of arsenic exposure, which will be discussed in Section 3.

Epigenetic changes

While studies have identified DNA repair deficiency as a mechanism of arsenic carcinogenesis, epigenetic regulation contributes to changes in DNA repair after arsenic exposure. Decreased gene expression is an established effect of arsenic exposure and studies show arsenic alters DNA methylation patterns across the genome with some sex differences (Bailey et al., 2013; Broberg et al., 2014; Nohara et al., 2011). Increased methylation of promotors involved in DNA repair has been associated with modified expression after arsenic exposure and was observed across different repair pathways. For example, BRCA1, ERCC2, MLH1, and OGG1 all had increased promoter methylation after arsenic exposure often associated with decreased expression (Hossain et al., 2012; Paul et al., 2014; Selmin et al., 2019; Wang et al., 2021). These studies support the finding that DNA methylation is associated with persistent genomic instability (Mauro et al., 2015). Confirming the importance of these finding are studies showing altered methylation patterns in populations exposed to arsenic (Bhattacharjee et al., 2018; Intarasunanont et al., 2012).

DNA methylation may be affected by the metabolism of arsenic, which involved methylation steps. Long term arsenic exposure has been associated with DNA hypomethylation as a result of depleted S-adenosylmethionine (SAM) (Reichard et al., 2007). While the mechanisms are not fully understood, SAM depletion results in decreased DNA methyltransferase activity, which may contribute to this effect (Du et al., 2018). Depletion of SAM and methylation activity may also affect histone methylation.

Posttranslational histone modifications, including methylation and acetylation, play an important role in gene expression. Arsenic has been shown to affect each of these posttranslational modifications creating a complicated landscape for understanding how they alter gene expression and accessibility and recruitment of DNA repair factors to sites of DNA damage. One study found the altered balance of H3K9me2, H3K36me3

and H4K20me2 after arsenic exposure may lead to decreased repair ability at sites of DNA damage (Li et al., 2016). Directly related to expression of DNA repair genes, arsenic increased H3K9me2 was found to reduced expression of genes involved in BER (Ding et al., 2021). Other studies show global histone methylation patterns after arsenic exposure are a contributing factor in malignant transformation (Ge et al., 2018) and cell transformation (Qiu et al., 2021). Zhang et al., 2020 found histone demethylase JDHM2A is responsible for regulating H3K9 dimethylation after arsenic exposure as a potential mechanism.

Arsenic altered levels of histone acetylases may also contribute to changes in gene expression, especially of DNA repair genes. H3K18ac was downregulated after arsenic exposure and this effect was notable in the promoter regions of NER protein genes (Zhang et al., 2020). Arsenic may also inhibit accessibility to repair sites of DNA damage through decreased histone acetylation. For example, arsenic decreased global H4K16Ac, notable for its role in relaxing chromatin, with concentration and time (Jo et al., 2009). Mechanisms of altered histone acetylation, including the effect of arsenic on histone acetyltransferases following arsenic exposure has been linked to zinc finger protein interactions (Tam et al., 2017).

Epigenetic alteration of gene expression is also affected by arsenic-induced changes in microRNAs, which have been linked to inhibited DNA repair, increased sensitivity to oxidative stress, and cellular transformation, and have been proposed to be used as biomarkers of arsenic exposure (Sturchio et al., 2014). Various cohorts of arsenic exposed people around the world have been evaluated for changes in microRNA expression to understand which microRNAs may be playing a role in disease progression (Al-Eryani et al., 2018a; Banerjee et al., 2019; Beck et al., 2018; Ruiz-Vera et al., 2019). Specific microRNAs have been linked with arsenic-induced skin lesions and cancers. For example, Banerjee et al., 2017 found miR-21 contributes to skin lesion and cancer in chronically exposed individuals.

Cell culture studies have looked closely at the role of specific microRNAs altered by arsenic exposure in targeted pathways of cancers. A study of prolonged exposure to arsenic used HaCaT cells as a model for skin cancer and identified dynamic changes in microRNA expression at different stages of exposure and transformation (Banerjee et al., 2022). Looking at specific microRNAs, Gonzalez et al., 2015 found arsenic upregulated miR-21, miR-200a, and miR-141 expression, and determined a likely association with pathways of melanoma progression. Another cell culture study found miR-200b was associated with malignant transformation of bronchial epithelial cells (Wang et al., 2011). These studies have investigated associations between microRNAs and cellular transformation and carcinogenesis. Others have focused on earlier processes in arsenic carcinogenesis. For example, arsenic altered microRNAs were implicated in targeting specific pathways such as the TP53 pathway, implicated to have early effects contributing to carcinogenesis (Al-Eryani et al., 2018b). An *in vivo* study in rats found arsenic-responsive microRNAs are likely involved in pathways of oxidative stress, specifically related to genes that regulate GSH levels (Ren et al., 2015).

MicroRNA studies in human populations and in experimental models have been used to understand how they may affect DNA repair. For example, Wei et al., 2018 found miR-145 was upregulated in individuals exposed to toxic levels of arsenic, and this effect was replicated in a cell culture model where it was found to target expression of ERCC2, potentially having a negative impact on DNA repair. From these studies it is likely microRNAs play a role in pathways of arsenic-induced carcinogenesis and modulating expression DNA repair genes.

Protein Effects

Arsenic-dependent changes to protein expression were discussed above. However, arsenic also affects protein directly. Recent studies have focused on how arsenic affects protein folding signaling pathways and protein function. For example, arsenic induced endoplasmic reticulum protein folding stress, which contributed to autophagy defects but not oxidative stress suggesting this effect is independent of ROS (Dodson et al., 2018). Endoplasmic reticulum protein folding effects have been observed in other arsenic studies as well and is associated with autophagy (Wadgaonkar and Chen, 2021).

While arsenic-altered protein expression and processing contribute to carcinogenic mechanisms, studies show arsenic can interact with zinc finger proteins causing inhibited function, and as briefly mentioned in Section 1, has a significant effect on zinc finger protein interactions. Zinc finger proteins are highly sensitive to oxidation due to thiol groups that play a central role in their function (Krishna et al., 2003). This structure is protected and maintained by a zinc ion, which coordinates a combination of 4 cysteine and histidine residues within the zinc finger domain. Zinc fingers can be found in several arrangements of cysteine and histidine including C2H2, C3H1, C4 and more complex structures like C4C4 ring domains (Klug et al., 2010; Razin et al., 2012). These structures are largely responsible for protein binding nucleic acids and with other proteins (Eom et al., 2016; Fu and Blackshear, 2017).

The mechanisms of arsenic disruption of zinc finger proteins involves the direct displacement of zinc by arsenic within the zinc finger domain. However, different forms of arsenic bind the specific zinc finger orientations depending on the ratio of cysteine and histidine. In general, arsenic has a lower binding affinity for protein with one or two cysteines compared to those with three or four (Asmuss et al., 2000; Kitchin and Wallace, 2006a; Kitchen and Wallace, 2006b). However, while arsenite and arsenic trioxide show a preference to bind to C3H1 and C4 zing finger domains methylated arsenic can bind to all three C2H2, C3H1, and C4 types (Zhou et al., 2014). Details of specific forms of arsenic in carcinogenic mechanisms is discussed in Section 3. Arsenic is similar enough to zinc to competitively displace it from the zinc finger, but in doing so induces a conformational shift within the domain altering how the protein functions (Quintal et al., 2011). The selectivity of different forms of arsenic to bind zinc finger domains with specific combinations of cysteine and histidine also suggests binding selectivity and may impact specific carcinogenic mechanisms differently.

Arsenic displacement of zinc has significant implications for protein in many cell regulatory pathways affecting DNA repair and gene expression (Huestis et al., 2016; Zhou et al.,

2020a). Many studies have focused on the impact of arsenic on zinc finger proteins involved in DNA repair (Cooper et al., 2014; Ding et al., 2017; Tam et al., 2020; Zhou et al., 2011; Zhou et al., 2015). After DNA damage, repair proteins must form complexes around the damage site, which requires binding to the damaged DNA. DNA-binding proteins use zinc fingers for this purpose, and therefore if disrupted, can destabilize DNA repair complexes at sites of damage and inhibit repair. The DNA repair protein PARP-1 is a C3H1 zinc finger DNA binding protein shown to be a sensitive target of arsenic exposure inhibiting its function (Ding et al., 2009; Walter et al., 2007). This disruption interferes with DNA binding and recruitment of other DNA repair factors involved in different pathways of repair including NER and BER (Chaudhuri et al., 2017). Arsenic was also found to bind and displace zinc in XPA, a critical DNA repair factor in NER (Huestis et al., 2016).

Arsenic may impact DNA repair by modulating access to sites of DNA damage. Zhang et al., 2014 found arsenic was able to bind to RNF20 and RNF40 RING finger domains causing a conformational shift in these proteins. The RNF20 and RNF40 RING fingers are responsible for the monoubiquitinating histone H2B and promoting access of DNA double strand break repair factors to sights of DNA damage (Zhang et al., 2014). Indeed, Recruitment of DNA repair factors including the HR repair protein, RAD51, to sites of double strand breaks was impaired after arsenic exposure. Similarly, arsenic was found to bind the FANCL E3 ubiquitin ligase and RING finger protein, altering recruitment of DNA repair factors to sites of DNA interstrand crosslinks (Jiang et al., 2017). These studies demonstrate arsenic can impact the function of different types of zinc finger proteins. Additionally, this interference affects different mechanisms of DNA damage repair and recruitment highlighting the dynamic and vast effect arsenic can have on cellular processes.

Signaling Pathways

Altered signaling after arsenic exposure contributes to checkpoint control, DNA repair response, and cell survival changes linking them together. Many pathways altered by arsenic exposure are interconnected and likely affect multiple mechanisms of arsenic carcinogenesis. One study using arsenic as a case study predicted top pathways associated with arsenic exposure include stress response, apoptosis, cell cycle, and protein signaling pathways such as MAPK, Jak-STAT, and p53 (Davis et al., 2008). MAPK signaling disruption has been observed in cell culture studies to increase cell invasiveness (Tingting et al., 2010). Predictions on arsenic's effect in signaling pathways including JNK, EGFR, AKT, PI3L, mTOR, and Nrf2-Keap1 have been extensively validated in other studies as well (Chen et al., 2013; Kang and Lee, 2008; Fu et al., 2021; Wang et al., 2017). These pathways are interconnected but are largely related to cell survival and escape from cell death and transformation.

The EGFR pathway has been closely linked with alterations of DNA repair and cell proliferation after arsenic exposure. Tong et al., 2015 found DNA mismatch repair was inhibited after arsenic exposure by promoting EGFR expression. Another study found EGFR and HB-EGF were activated in arsenic-transformed cells to promote cell proliferation (Wang et al., 2020). Recently a study in lung epithelial cells found EGFR expression was enhanced

after acute and chronic arsenic exposure, but the mechanism responsible for these changes was different depending on the exposure time (Kim et al., 2020).

The balance of cell survival and cell death pathways are shifted after arsenic exposure (Dreval et al., 2018; Watcharasit et al., 2012). The Nrf2-Keap1 signaling pathway is a cellular mechanism implicated in promoting cell survival and when dysregulated is considered to have cancer-promoting functions. Specifically, constitutively active Nrf2 leads to a variety of downstream implications including altered expression of growth factors, antioxidant proteins, transcription factors, and protein processing due to its activity in binding antioxidant response elements (AREs) in the promoter of genes (Hayes et al., 2010). Studies show arsenic constitutively activates Nrf2 is closely tied to the alteration of the autophagy pathway (Lau et al., 2013; Zhou et al., 2020b). Indeed, studies show arsenic increases autophagy activity (Bolt et al., 2010; Pucer et al., 2010).

Many studies have investigated the PI3K AKT, and mTOR pathways in arsenic cellular transformation and malignancy (Chen and Costa, 2018). When these pathways are unregulated normal cell growth becomes aberrant. Chronic arsenic exposure alters the PI3K/AKT pathway and is associated with anchorage-independent growth and cell migration (Carpenter and Jiang, 2013). Other studies have found autophagy dysfunction is tied to PI3K and mTOR signaling (Liang et al., 2020). Evidence shows in arsenic-transformed cells the AKT pathway is implicated in enhancing invasiveness (Wang et al., 2012) while being regulated upstream by JNK to promote alterations in phosphorylation of proteins involved in altering expression of tumor suppressors and oncogenes (Chen et al., 2013).

SECTION 3: CHEMICAL FORMS OF ARSENIC AND CARCINOGENESIS

Inorganic and Organic Arsenic Forms, Exposure, and Metabolism

Arsenic exists in several different oxidation states and various chemical forms (Carlin at al., 2016; Bolt and Henglestler, 2018). There are two major oxidation states of arsenicals, trivalent and pentavalent. Both oxidation states exist naturally (Carlin at al., 2016; Zhu et al., 2014). Arsenic occurs naturally in many minerals, usually in combination with sulfur and metals. Humans can be exposed to arsenic through different forms and oxidation states, and metabolism of arsenic also converts one form or oxidation state to another (Watanabe and Hirano, 2013). Each form/oxidation state may have different exposure routes, organ/tissue distribution, toxicity, and carcinogenic effects (Watanabe and Hirano, 2013; Sattar et al., 2016). There are two major forms of arsenicals, inorganic and organic. Inorganic arsenicals are the major form of arsenic exposure, occupationally and environmentally. Organic arsenicals are mainly acknowledged as metabolites of arsenic, specifically, in methylated forms (Negro Silva et al., 2017; Cohen et al. 2006).

Trivalent arsenicals are found in the form of sodium/potassium arsenite and arsenic trioxide (Dopp et al., 2005). Pentavalent arsenicals are mainly found as sodium arsenate. The environmental existence of inorganic arsenicals is in two major phases, solid and a liquid. Inorganic arsenicals in ground water can be found in both trivalent and pentavalent forms (Zheng et al., 2017). The trivalent and pentavalent forms mainly exist in oxic and anoxic

waters, respectively, due to their chemical properties. Drinking water is a major source of environmental exposure of inorganic arsenicals (Carlin at al., 2016; Zhu et al., 2014; Mantha et al., 2017). As mentioned in Section 1 arsenicals may also be accumulated in plants through irrigation (Zhu et al., 2014; Mantha et al., 2017; Dominguez-Gonzales et al., 2020), such as rice and vegetables, which also serve as a significant source of inorganic arsenic exposures. Trivalent and pentavalent arsenicals also exist in soil which leads to inhalation exposure from dust (Liu et al., 2016, Alamdar et al., 2016). Occupational exposure of arsenic can occur in facilities that manufacture pesticides, herbicides, and other agricultural products (Baker et al., 2018). Mine smelters and woodworking facilities are also major sources of occupational inorganic arsenic exposures.

Organic arsenicals are not commonly found naturally in the environment. Organic arsenicals include arsanilic acid, arsenosugars, and methylated arsenicals. Methylated arsenicals are produced as a consequence of inorganic arsenic biotransformation in various organisms. Humans may be exposed to methylated arsenicals from ingestion of seafood and meat (Yoshinaga and Narukawa, 2021; Naess et al., 2020).

Trivalent arsenic uptake into eukaryotes is mediated mainly by proteins in the aquaporin superfamily (AQPs) (Agre et al., 2002). Mammalian AQPs were first identified to transport trivalent arsenic in rat and mice as AQP9 and AQP7, respectively (Liu et al., 2002). Meanwhile, trivalent arsenic has also been shown to be taken up by glucose transporters such as GLUT1 (Liu et al., 2006) and hexose permeases (Liu et al., 2004). Both aquaglyceroporins and glucose permeases are bidirectional routes of trivalent arsenic into and out of cells.

Organic arsenic forms contribute to arsenic toxicity mainly through metabolic pathways. The metabolism of arsenic after absorption consists of two major types of reactions; oxidative methylation and reduction (Li et al., 2017; Hughes et al., 2011) (Figure 4). First, arsenite is oxidatively methylated into monomethylarsonic acid (MMA^V). MMA^V is thus reduced into monomethylarsonous acid (MMA^{III}). Second, MMA^{III} is oxidatively methylated into dimethylarsonic acid (DMA^V), then reduced into dimethylarsonous acid (DMA^{III}). The metabolism of arsenic plays a critical role in toxicity and carcinogenesis. The exact mechanisms of action of different arsenic forms is still unclear, but various hypotheses have been proposed.

Under drinking water exposure, an animal study of organ distribution of arsenicals suggested that kidney, lung and liver contain highest levels of arsenic (Li et al., 2013). In lung, the major form is DMA^{III} at almost all time points (Kenyon et al., 2005). At early stages of exposure, liver and kidney contain all forms of arsenicals, such as MMA^{III}, MMA^V, DMA^{III}, DMA^V, and inorganic arsenic. At later stages, both liver and kidney show an increase in the percentage of DMA^{III} in arsenicals (Kenyon et al., 2005). In contrast, blood and brain contains the lowest level of all arsenic forms compared to other organs across all time points. Inorganic and organic arsenicals were also reported to be strongly accumulated in reproductive organs (Pant et al., 2004).

The subcellular distribution of arsenicals largely depends on the cell type. According to the characteristics of arsenic metabolism, there are two different types of cells, methylating (such as hepatocytes) and non-methylating (such as urothelial cells) (Dopp et al., 2010). The membrane permeability and the efficacy of arsenic uptake depend upon both the arsenic species and the cell type (Dopp et al., 2005). Uptake rates of MMA^{III} and DMA^{III} were highest and exceeded those of their pentavalent counterparts by several orders of magnitude. Non-methylating cells accumulate higher amounts of arsenic within the cell than the methylating cells, and cellular uptake and efflux seem to be faster in methylating cells. Elevated concentrations of arsenic are present in the ribosomal fraction of non-methylating cells and in nucleic and mitochondrial fractions of methylating cells. However, cytotoxic and genotoxic effects are more pronounced in methylating cells (Dopp et al. 2008), which also suggests that methylated forms of arsenic may have greater cytotoxic effects than inorganic arsenic forms.

Carcinogenesis of Arsenic Forms

Arsenic exposure is mainly in the form of trivalent inorganic arsenic through gastrointestinal absorption. Different forms and oxidation state of arsenicals play various roles in carcinogenesis (Wadgaonkar and Chen, 2021). Some research indicates that organic arsenic forms such as MMA and DMA are most relevant to skin and bladder cancers (Gamboa-Loira et al., 2017). MMA and DMA are both positively related to almost all types of cancers (Gamboa-Loira et al., 2017; Di Giovanni et al., 2020; Kuo et al., 2017; Jomova et al., 2011). However, DMA level was found to be negatively correlated to lung cancer only (Gamboa-Loira et al., 2017).

MMA^{III} induces malignant transformation in a human bladder urothelial cell line (Bredfeldt et al., 2006), and this kind of transformation is irreversible (Wnek et al., 2010). Acute and chronic MMA^{III} exposure induces MAPK and COX-2, which may be a mechanism of bladder carcinogenesis (Eblin et al., 2007). Also, MMA^{III} alters histone modification patterns in human bladder cells (Ge et al., 2018). There are still gaps in research progress on organic arsenic forms and liver and lung cancers.

The molecular mechanisms of arsenic induction of various cancers can be summarized into two major categories: a) the trivalent arsenicals activate or inhibit signaling proteins or alter protein structure by reacting with proteinaceous thiol groups and b) inorganic or organic arsenicals activate ROS signaling or ROS-related signaling pathways. Carcinogenesis of inorganic arsenicals is related to both mechanisms. However, organic arsenicals are predominantly reported to correspond to ROS-dependent mechanisms at present (Huang et al., 2017). Current literature suggests that both inorganic and organic arsenicals contribute to arsenic carcinogenesis. It remains to be determined which specific form of arsenic is the most carcinogenic, although the answer may likely depend on the chemical properties of arsenical and the target organ.

Forms of Arsenic and Reactive Oxygen Species

Almost all forms and oxidation states of arsenicals can induce ROS and relevant signaling pathways (Lee et al., 2016). For example, for arsenic trioxide, superoxide induction occurs

through HO-1, hydrogen peroxide and also RNS such as nitric oxide and peroxynitrite (Zhou et al., 2019; Chen et al., 2008; Gurr et al., 2003). In murine embryonic maxillary mesenchymal cells, pentavalent arsenic leads to oxidative injury initiating cell death cascade, triggering cytotoxicity, mitochondrial dysfunction, and activation of caspase-9 (Singh et al., 2010). Specifically, the antioxidant N-acetylcysteine attenuates the effect of pentavalent arsenic, suggesting that ROS production may contribute to the mechanism of pentavalent arsenic cytotoxicity.

In human bladder urothelial cells, MMA^{III} is known to produce ROS (Wnek et al., 2011). In smooth muscle cells, MMA^{III} has been reported as a mitochondria toxicant that elevates ROS through mitochondrial and non-mitochondrial pathways (Pace et al., 2016). In rat liver cells, MMA^{III} has the highest potential of ROS generation, followed by DMA^{III}, then arsenic trioxide (Naranmandura et al., 2011). In human bladder urothelial cells, MMA^{III} was also observed to generate higher ROS than the same concentration of arsenic trioxide (Eblin et al., 2006). In human myeloid leukemic HL-60 cells, MMA^{III} and DMA^{III} cause apoptosis through inhibition to mitochondrial membrane potential and oxidative stress (Rehman et al., 2014). Caspase-9 and caspase-3 were significantly activated by MMA^{III} and DMA^{III} exposure. Similarly, antioxidant N-acetylcysteine is also able to reverse these effects (Rehman et al., 2014).

In HepG2 cells, MMA^{V}, DMA^{V}, or trimethylarsine (TMA^{V}) significantly induced CYP1A1 and NQO1 through an Hsp90 pathway (Anwar-Mohamed et al., 2014). ROS production by MMA^{V} exposure is also significantly higher than arsenic trioxide. Overall, MMA^{V} and DMA^{V} have moderate effect when compared to MMA^{III} and DMA^{III}, but the effects become stronger in a reductive environment, for example when there is a low ROS/GSH ratio (Sakurai et al., 2005).

In total, inorganic and organic arsenicals both contribute to ROS generation and ROS-dependent signaling pathways. However, there are still debates on which arsenic form generates higher ROS *in vivo*. It is still largely unclear whether metabolism of arsenic could enhance or reduce the strength of ROS effect. In addition, there is still limited knowledge on the differences of ROS type generated from different arsenicals, which should be of importance to ROS-related mechanisms.

Forms of Arsenic and DNA Damage/Repair

As mentioned in Section 2, trivalent arsenic inhibits DNA repair through direct interaction with zinc finger DNA repair proteins such as PARP-1 and XPA. For pentavalent arsenicals, there is no evidence currently demonstrating direct interaction with zinc fingers. However, pentavalent arsenicals are able to generate ROS which are not only able to induce DNA damage but also impair DNA repair pathways (Flora, 2011; Schwerdtle et al., 2003). Therefore, in contrast to trivalent arsenicals, which inhibit DNA repair through both direct and ROS pathways, pentavalent arsenicals inhibit DNA repair only through ROS-dependent signaling pathways.

In natural killer cells, at low concentration, MMA^{III} induces oxidative stress, DNA damage, and inhibits cell growth. DNA damage positively correlates with oxidative stress, indicating

that at environmentally relevant concentrations, MMA^{III} has a genotoxic effect (Xu and Wang, 2018). In human bladder urothelial cells, low-level chronic exposure to MMA^{III} elevates DNA damage, which remains at a high level after removal of MMA^{III}, and elevated levels of ROS also play a role in MMA^{III} induced-DNA damage (Wnek et al., 2009). While pentavalent arsenicals only act through ROS-dependent pathways, MMA^{III} has two potential interdependent mechanisms for human bladder urothelial cell transformation; elevated levels of MMA^{III}-induced DNA damage through the production of ROS and the direct MMA^{III}-induced inhibition of PARP-1 (Wnek et al., 2011), which has been confirmed *in vitro* (Zhou et al., 2014).

In T cells, MMA^{III} induces strong genotoxicity in the early developing T cells in the thymus. In terms of MMA^{III} induced genotoxicity and apoptosis, double negative ($CD4^{-}$ $CD8^{-}$) T cells were much more sensitive than double positive cells (Xu et al., 2017). ROS-dependent mechanisms are particularly important. For example, superoxide is involved either directly or indirectly in producing DNA damage in cells exposed to trivalent methylated arsenicals. DMA^{III} and MMA^{III} produced significantly more DNA damage in the homozygous knockout mouse splenocytes than in the splenocytes from the wild-type or heterozygous mice (Tennant and Kligerman, 2011).

Overall, the DNA damage effect and DNA repair inhibition capabilities of various arsenic forms and oxidative states largely depend on the tissue or cell type. Intriguingly, in bladder or human urothelial cells, DMA^{III} and MMA^{III} are the most hazardous arsenicals when considering cytotoxicity and genotoxicity (Bailey et al., 2012; Wang et al., 2007). However, in lung and skin cells, trivalent arsenicals show higher potency for DNA damage (Bolt and Hengstler, 2018; Sattar et al., 2016). This may be because of a difference in metabolism or cellular arsenic uptake.

Conclusion

There is extensive and strong epidemiological evidence that links arsenic exposure with increased risk of developing various types of cancer. Arsenic is ranked number one by the Agency for Toxic Substances and Disease Registry (ATSDR) on their priority list of substances that are determined to pose the most significant potential threat to human health. The most effective and efficient strategy to decrease arsenic-induced cancer risk is to reduce arsenic exposure. Based on convincing research findings, in 2001, U.S. EPA adopted a new standard for arsenic in drinking water of 0.01 mg/l or 10 parts per billion (ppb), replacing the old standard of 50 ppb. The same standard has since been used by most countries around the world. However, it is estimated that over 200 million people world-wide remain exposed to arsenic above this level (Li and Costa 2022).

Over the last several decades, extensive research has been carried out to investigate and identify various molecular and cellular changes caused by arsenic that are associated with known carcinogenic processes. Despite tremendous progress to date, we still do not fully understand exactly how arsenic causes cancer development, and what are the key cancer-driving events that play critical roles in arsenic-induced cancer. One of the significant barriers in research is the lack of relevant and appropriate animal models that mimic the

development of arsenic-induced cancer in humans, probably due to differences in genetics and arsenic metabolism between rodents and humans. Recent development in humanized mice could potentially provide an important tool to help resolve these critical questions (Koller et al., 2020).

Another major issue is that while current research has identified many individual molecular targets of arsenic involved in carcinogenic processes, it is difficult to assess which of these altered processes are predominantly responsible for arsenic-induced cancer in humans. The recent advances in whole genome sequencing and the associated informatics technology could help identify, using unbiased approaches, target molecules and processes that drive the mutation and tumorigenesis at the whole genome level.

Abbreviations

8-OHdG	8-hydroxy-2’-deoxyguanosine
AQP	aquaporin
AS3MT	arsenic methyltransferase
ATSDR	Agency for Toxic Substances and Disease Registry
BER	base excision repair
CPD	cyclobutene pyrimidine dimer
DMA	Dimethylated arsenic
DMA^{III}	dimethylarsonous acid
DMA^{V}	dimethylarsonic acid
EPA	US Environmental Protection Agency
GSH	glutathione
HR	homologous recombination
IARC	International Agency for Research on Cancer
MMA	Monomethylated arsenic
MMA^{III}	monomethylarsonous acid
MMA^{V}	monomethylarsonic acid
NER	nucleotide excision repair
NHEJ	non-homologous end joining
NOX	NADPH oxidase
PAH	polyaromatic hydrocarbons

RNS	Reactive nitrogen species
ROS	Reactive oxygen species
TMA(V)	trimethylarsine
UVR	ultraviolet radiation
WHO	World Health Organization

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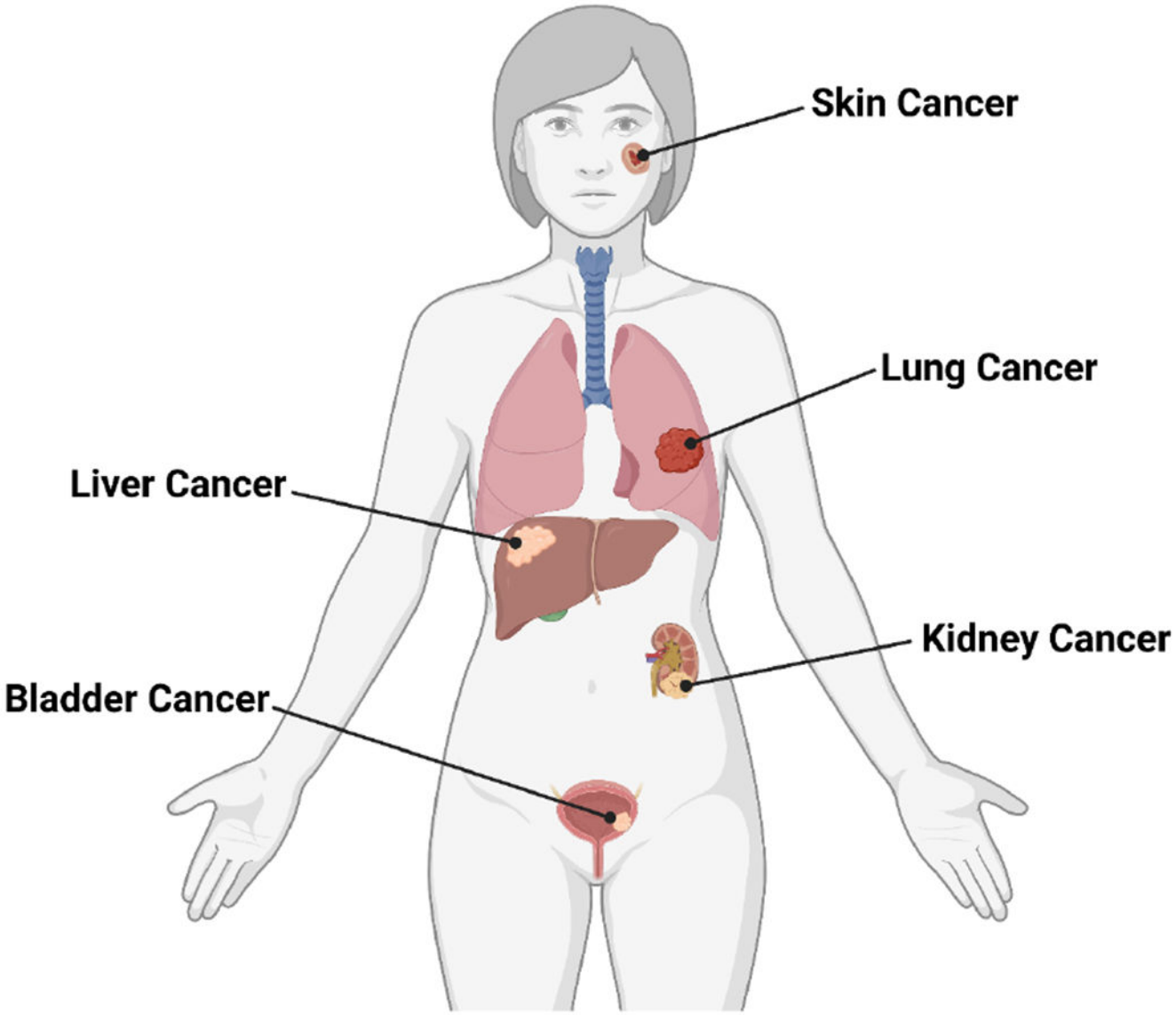

Figure 1.

Cancers associated with arsenic exposure. Epidemiology studies support the association of arsenic exposure through drinking water with increased risk of developing skin, lung, bladder, kidney, and liver cancers.

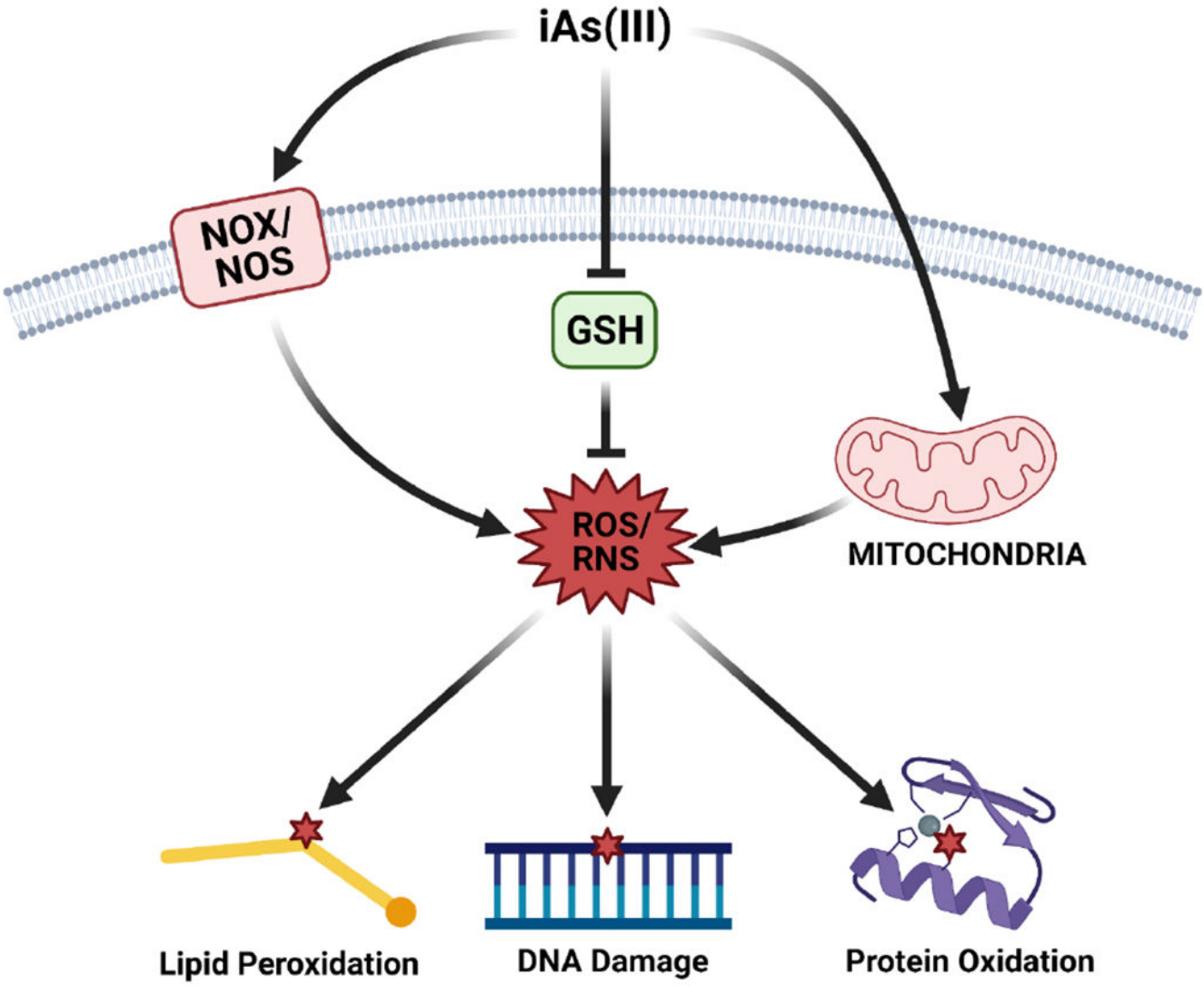

Figure 2. Mechanism of arsenic-induced ROS and oxidative damage to macromolecules.

Arsenic exposure stimulates the production of ROS and RNS through mechanisms such as the dysregulation of the electron transport chain and stimulation of enzymes such as NADPH oxidase and nitric oxide synthase. The depletion of GSH through the metabolism of arsenic further promotes redox imbalance. Consequently, macromolecules such as DNA, protein, and lipids are damaged by arsenic-induced ROS and RNS.

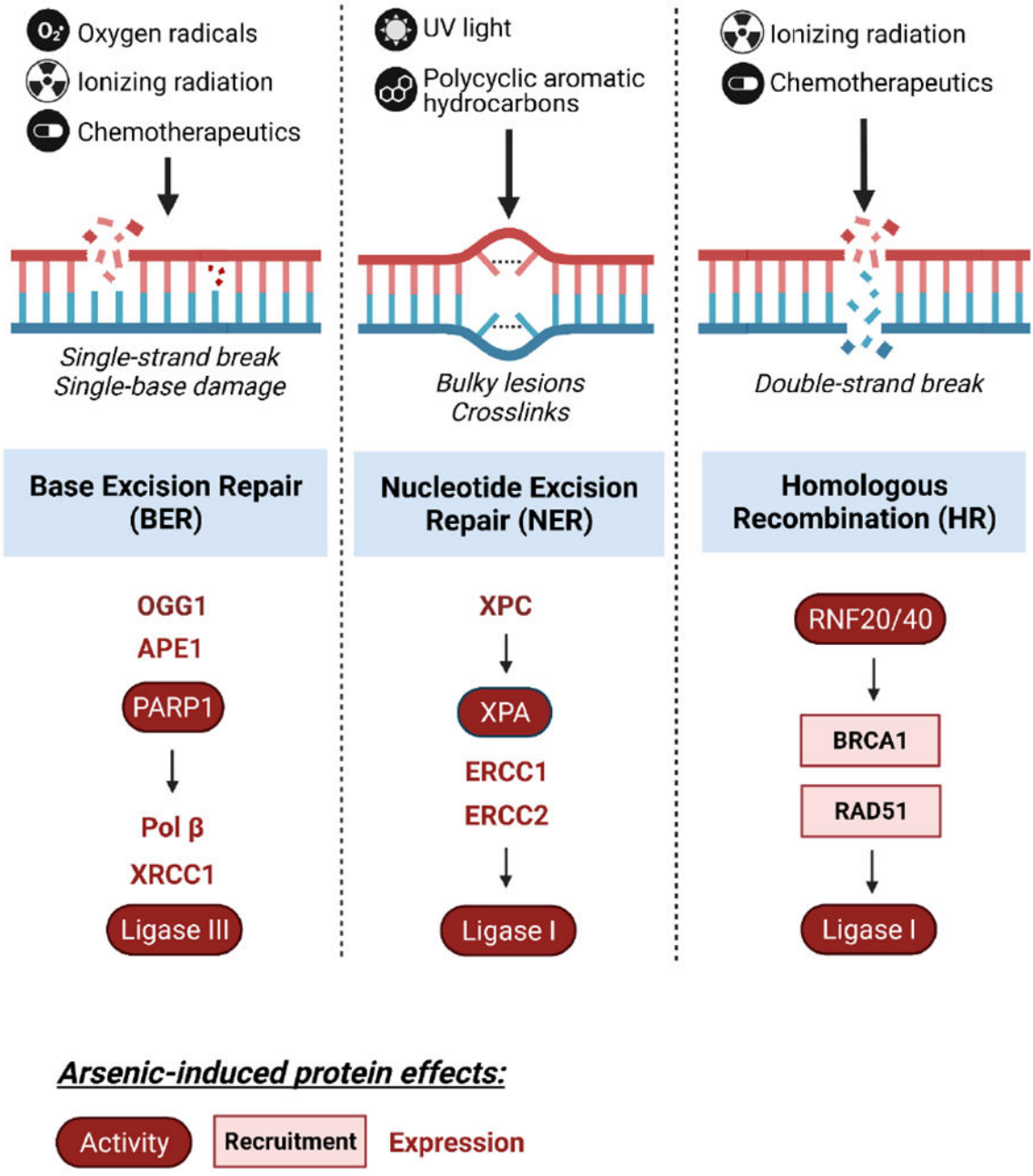

Figure 3. Arsenic inhibits DNA repair.

Exposure to DNA damaging agents such as ROS, UV light, and ionizing radiation can generate single-base damage, bulky lesions, and double-strand breaks, respectively. These types of damage are remediated by repair pathways which contain critical DNA repair proteins that facilitate the recruitment of repair proteins, removal of damage, and the synthesis and sealing of undamaged DNA. Arsenic alters the function of key DNA repair proteins through several means: zinc finger domain inhibition leading to loss of activity,

disruption in recruitment to DNA damage, and the suppression of expression by altering transcription and protein turnover.

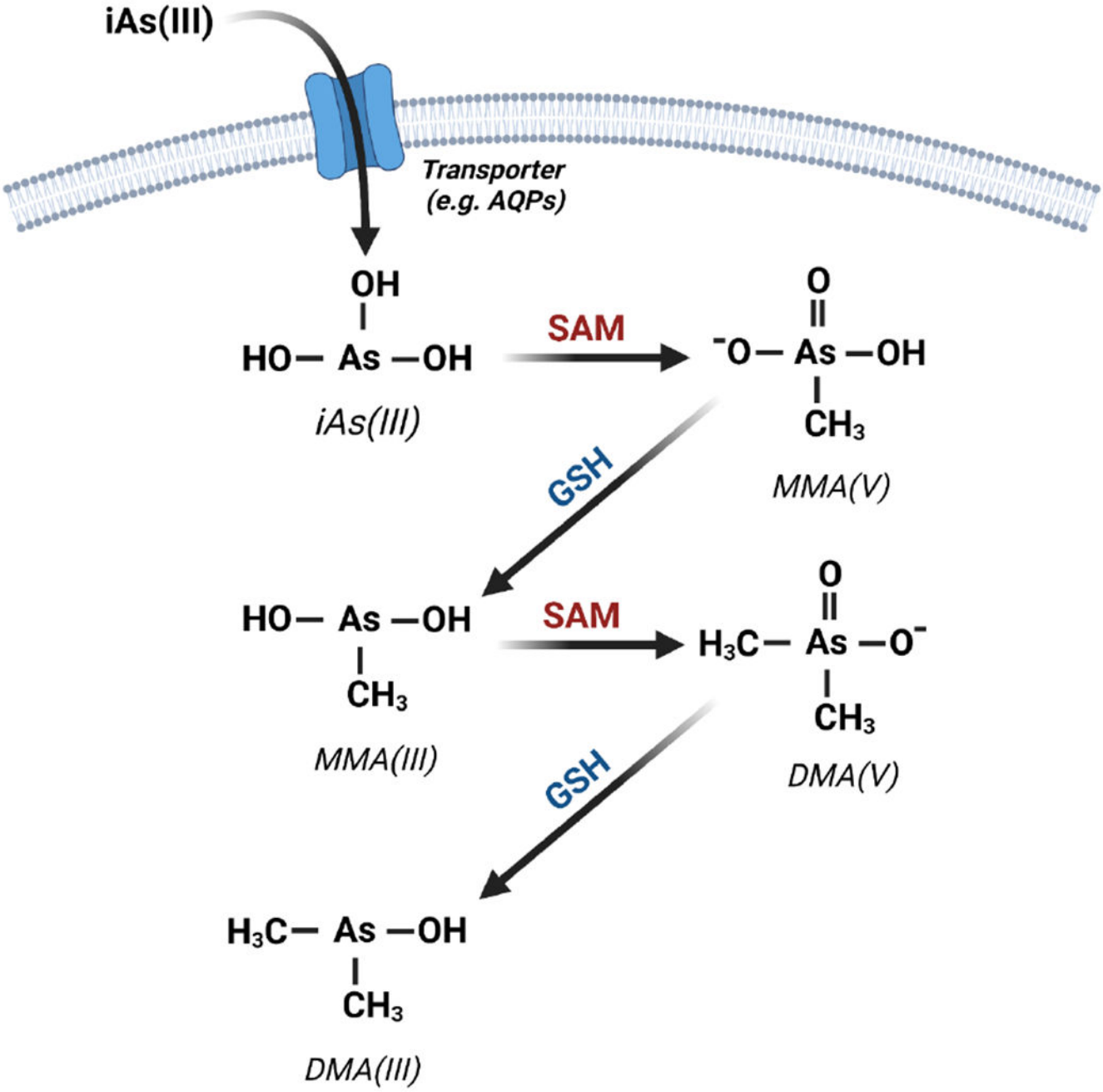

Figure 4.

The metabolism of arsenic. The uptake of trivalent arsenic into eukaryotes is mediated through several transporters such as AQPs. Trivalent arsenic is metabolized by successive oxidative methylation and reduction reactions. First, iAs(III) is oxidatively methylated into MMA(V) by S-adenosyl methionine (SAM), then reduced into MMA(III) by GSH. Second, MMA(III) is oxidatively methylated into DMA(V), then reduced into DMA(III)

Exhibit J

A Section 508–conformant HTML version of this article is available at http://dx.doi.org/10.1289/ehp.1510144.

Estimating Children's Soil/Dust Ingestion Rates through Retrospective Analyses of Blood Lead Biomonitoring from the Bunker Hill Superfund Site in Idaho

Ian von Lindern,[1] Susan Spalinger,[1] Marc L. Stifelman,[2] Lindsay Wichers Stanek,[3] and Casey Bartrem[1]

[1]TerraGraphics Environmental Engineering, Inc., Moscow, Idaho, USA; [2]U.S. Environmental Protection Agency (EPA), Region 10, Seattle, Washington, USA; [3]U.S. EPA, Office of Research and Development, Research Triangle Park, North Carolina, USA

Background: Soil/dust ingestion rates are important variables in assessing children's health risks in contaminated environments. Current estimates are based largely on soil tracer methodology, which is limited by analytical uncertainty, small sample size, and short study duration.

Objectives: The objective was to estimate site-specific soil/dust ingestion rates through reevaluation of the lead absorption dose–response relationship using new bioavailability data from the Bunker Hill Mining and Metallurgical Complex Superfund Site (BHSS) in Idaho, USA.

Methods: The U.S. Environmental Protection Agency (EPA) *in vitro* bioavailability methodology was applied to archived BHSS soil and dust samples. Using age-specific biokinetic slope factors, we related bioavailable lead from these sources to children's blood lead levels (BLLs) monitored during cleanup from 1988 through 2002. Quantitative regression analyses and exposure assessment guidance were used to develop candidate soil/dust source partition scenarios estimating lead intake, allowing estimation of age-specific soil/dust ingestion rates. These ingestion rate and bioavailability estimates were simultaneously applied to the U.S. EPA Integrated Exposure Uptake Biokinetic Model for Lead in Children to determine those combinations best approximating observed BLLs.

Results: Absolute soil and house dust bioavailability averaged 33% (SD ± 4%) and 28% (SD ± 6%), respectively. Estimated BHSS age-specific soil/dust ingestion rates are 86–94 mg/day for 6-month- to 2-year-old children and 51–67 mg/day for 2- to 9-year-old children.

Conclusions: Soil/dust ingestion rate estimates for 1- to 9-year-old children at the BHSS are lower than those commonly used in human health risk assessment. A substantial component of children's exposure comes from sources beyond the immediate home environment.

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Introduction

Ingestion Rate Background

Consumption of fine soil and dust particulates, especially by young children, is the dominant route of exposure for lead and other contaminants (Laidlaw et al. 2014; Landrigan et al. 1975; Lanphear et al. 1998, 2003). Childhood soil and dust ingestion occurs via multiple pathways, including hand-to-mouth transfer, mouthing of objects, and contaminated food. These pathways are dependent on individual behaviors, exposure time, and environmental conditions (Zahran et al. 2013a). Accurate estimates of the soil and household dust ingestion rate (IR) pathway are needed to assess children's exposures and health risks associated with trace metals and persistent organic chemical residues in the home or play environment, and to make informed cleanup decisions.

Early estimates of soil/dust IRs in children were based on studies of trace elements in soil and feces, yielding uncertain estimates due to analytical uncertainty, limited sample size, and short study duration (Batelle 2005; Doyle et al. 2010; Sedman and Mahmood 1994; Stanek et al. 2012; U.S. EPA 2011, 2012). Currently, national U.S. Environmental Protection Agency (EPA) central tendency soil/dust IRs of 60 mg/day (children 6 weeks to < 12 months of age) and 100 mg/day (children 1 to < 6 years of age) are based on these tracer studies (U.S. EPA 2011). More recent studies have used dermal transfer to estimate soil and dust IRs. Ozkaynak et al. (2011) modeled the frequency of hand and object mouthing in children 3 years to < 6 years of age, resulting in a mean total soil/dust IR of 68 mg/day (95th percentile: 224 mg/day). Similarly, Wilson et al. (2013) used a mechanistic model including parameters for particle loading on skin, transfer to hands, hand surface area, mouthing surface area, hand-to-mouth frequency, saliva dissolution, and exposure time, to estimate an average combined soil/dust IR of 61 mg/day for children 7 months to 4 years of age. Meta-analysis of four major studies using stochastic modeling of the most reliable tracers resulted in an average soil ingestion estimate of 26 mg/day (95th percentile: 79 mg/day) for children 1–8 years of age (Stanek et al. 2012). Findings from large-scale reviews and integration of data from tracer, mechanistic, validation modeling/measurement, and empirical relation (biomonitoring/environmental concentration) studies suggest that mean IRs in children are < 100 mg/day and may be as low as 40–80 mg/day (Bierkens et al. 2011; Moya and Phillips 2014).

Soil/dust IR and bioavailability are sensitive parameters in the U.S. EPA Integrated Exposure Uptake Biokinetic (IEUBK) Model for Lead in Children. The IEUBK model currently uses default IRs ranging from 85 to 135 mg/day for 6-month- to 6-year-old children and 30% absolute bioavailability for ingested soil and indoor dust (U.S. EPA 2013). The first use of the IEUBK model to develop site-specific cleanup levels was at the Bunker Hill Mining and Metallurgical Complex Superfund Site (BHSS) in northern Idaho (CH2M Hill 1991; TerraGraphics 1990; U.S. EPA and IDHW 1991, 1992). The dose–response relationship observed between soil, dust, and blood lead levels (BLLs) was consistently lower at the BHSS than IEUBK model predictions using the default parameters (TerraGraphics 1990; von Lindern et al. 2003b). This was nominally attributed to lower soil/dust bioavailability (18%), although it was acknowledged that the reduced

Address correspondence to S. Spalinger, TerraGraphics Environmental Engineering, 121 S. Jackson St., Moscow, ID 83843 USA. Telephone: (208) 882-7858. E-mail: susan.spalinger@terragraphics.com

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I.v.L., S.S., and C.B. are employees of TerraGraphics Environmental Engineering, Inc., which is a consultant to the Idaho Department of Environmental Quality, and held two contracts at the time of this project for scientific and engineering support services for the Bunker Hill Superfund Site. TerraGraphics was also a consultant to U.S. EPA to conduct analyses for this research project. I.v.L. served on the U.S. Clean Air Science Advisory Committee for the Integrated Science Assessment for Lead in the Ambient Air and the Review of the Air Quality Criteria Document for Lead. C.B. and I.v.L. are also employed by TerraGraphics International Foundation, a nonprofit organization. The other authors declare they have no actual or potential competing financial interests.

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dose response was likely a combination of lower bioavailability and IRs (von Lindern et al. 2003b).

BHSS Background

In 1974, soon after the lead smelter operators bypassed emission controls destroyed by a baghouse fire, > 95% of children 1–9 years of age living within 3 mi of the smelter had BLLs exceeding 40 µg/dL (Yankel et al. 1977). Lead health interventions have been ongoing since that time. The smelter closed in 1981 and remediation began in 1986, representing one of the world's largest, most comprehensive, and well-documented lead health response cleanups (U.S. EPA 2005, 2010; von Lindern et al. 2003a, 2003b). From 1988 through 2002, soil from > 3,500 properties within the 21-mi^2 area surrounding the smelter was removed and replaced with up to 1 ft of clean fill averaging ≤ 50 mg/kg. Hundreds of families with children received lead health education and in-home follow-up investigations through a local Lead Health Intervention Program (LHIP). The LHIP tested children's BLLs, achieving participation rates > 50% among 0- to 9-year-old children for 15 consecutive years through door-to-door recruitment and incentive payments. Annual blood lead survey results were used to prioritize soil cleanup until the Remedial Action Objective (RAO) of < 5% of children with BLLs ≥ 10 µg/dL was achieved. From 1988 through 2002, homes of young children (0–6 years), pregnant women, and older children with BLLs ≥ 10 µg/dL were remediated first, regardless of location within the site. Beginning in 1994, all soils in contiguous neighborhoods with lead levels ≥ 1,000 mg/kg were removed and replaced, regardless of BLLs. This cleanup prioritization coupled with families moving within the affected communities resulted in a dynamic, complex combination of soil/dust exposures affecting individual children.

Blood lead data, collected during the seasonal peak in late summer, were matched to dust lead concentrations (from samples collected from household vacuum cleaners) and soil lead data to monitor the relationship between children's BLLs and environmental exposures to ensure cleanup was effective. Four variables were used to quantify soil and dust exposures throughout the cleanup: house dust, yard soil, neighborhood soil, and community soil lead concentrations. The neighborhood soil variable is the mean of all yard soils within a specific radius of the home, excluding the home's yard soil lead concentration. This was calculated for 200-ft, 500-ft, and 1,000-ft radii. The community soil variable is the mean of all yard soils within the community, excluding the home and neighborhood radius soil lead concentrations. The prioritized cleanup rapidly reduced the number of children residing in homes with soil lead concentrations ≥ 1,000 mg/kg and markedly decreased yard soil exposures for those families. Neighborhood soil lead concentrations progressively declined until the block-by-block cleanup strategy was implemented in 1994, and then decreased faster as contiguous neighborhoods were remediated. Community soil lead mean concentrations declined steadily until 2002 when yard soil replacement was mostly complete. House dust lead exposures (dust lead concentrations from homes of children with BLL measurements) decreased following the yard, neighborhood, community, and industrial complex cleanups but lagged the community soil means by a decade or more (von Lindern et al. 2003a).

By 2002, children's mean BLLs decreased to 2.2 µg/dL. In 2013, the health district conducted the first comprehensive blood lead survey since 2002, recruiting an estimated 50% of children 6 months to 9 years of age living within the 21-mi^2 area using incentive payments and door-to-door solicitation. The geometric mean BLL among 1- to 5-year-old children tested was 2.2 µg/dL (SD ± 1.8) compared with the most recent U.S. mean of 1.3 µg/dL (CDC 2013), with 2 of 276 children having levels ≥ 10 µg/dL, indicating that the cleanup continues to meet the RAO of 95% of children < 10 µg/dL (TerraGraphics 2015). Over the 15 years of active cleanup (1988–2002), education, and intervention, the LHIP amassed approximately 5,400 blood lead observations (referred to as the parent database) from nearly 2,340 individuals, yielding 2,176 records of blood/soil/dust lead concentrations (TerraGraphics 2004; von Lindern et al. 2003b, 2003a).

Subsequent to the cleanup at the BHSS, the U.S. EPA adopted an *in vitro* methodology to estimate site-specific bioavailability of lead in soil and dust (U.S. EPA 2012). This methodology was applied to a subset of archived soil and dust samples from the BHSS, and results were applied to the parent database. The objective of this study was to estimate age-specific soil/dust IRs through reanalysis of the dose–response relationship using new soil and house dust lead bioavailability data. In light of uncertainties and limitations of fecal tracer soil ingestion studies, these site-specific estimates likely have broader application to the IEUBK model and to human health risk assessment.

Methods

Blood lead samples collected from children participating in the LHIP were obtained through written informed consent from parents as well as child assent. The annual LHIP surveys are public health actions undertaken by state and local health authorities. TerraGraphics secured approval from the University of Idaho's Institutional Review Board for this project. No additional survey data or samples were collected from human subjects for this analysis.

Sample Analyses

In total, 271 samples (193 house dust samples, 73 yard soil samples, and 5 quality control samples) sieved to 80 mesh (or < 0.177 mm) were analyzed for total lead (Method 6010B) and *in vitro* bioaccessibility (TerraGraphics 2012; U.S. EPA 2007, 2012). U.S. EPA's *in vitro* assay measures the solubility, or bioaccessibility, of lead in soil and dust samples to estimate (*in vivo*) bioavailability. The 80 mesh sieve for both soil and dust was initiated at the BHSS in 1974 and focuses analyses on particle sizes more likely to adhere to hands and other surfaces and be ingested by children (Panhandle District Health Department et al. 1986; Ruby and Lowney 2012). Archived soil and dust samples collected between 1986 and 2002 were retrieved from storage. Those with intact seals, legible identification numbers, and sufficient mass for analysis were then checked to ensure that blood lead data and information on child age and sex, home location, and property remediation status were available. A temporal and geographic subset of samples meeting these criteria was randomly selected and analyzed at the laboratory. Reanalyzed soil and dust lead concentrations were compared to historical values using linear regression. *In vitro* bioaccessibility results were converted to *in vivo* relative bioavailability and absolute bioavailability (ABS) following U.S. EPA methods using comparison to a lead acetate reference (0.5) following Equation 1 (U.S. EPA 2007, 2009, 2012):

$$\mathrm{ABS} = (0.878 \times \mathrm{IVBA} - 0.028) \times 0.5, \quad [1]$$

where IVBA = *in vitro* bioaccessibility.

Community mean ABS values for unremediated yard soils and house dust, and site-wide ABS means for postremediation soils were integrated into the parent database. Annual site-wide ABS means were calculated using a weighted average of bioavailable lead (product of concentration and bioavailability) from remediated and unremediated yards.

Quantitative Analyses

Soil and dust partitions, age-specific IRs, and lead uptake from sources other than soil and dust were determined through structural equations modeling (SEM). SEM is a statistical multivariate methodology appropriate for pathways analysis, defined as a network of linear relations between variables. SEM was applied by von Lindern et al. (2003b) to reflect the exposure pathways of yard, community, and neighborhood soils (Ullman and Bentlar 2003). The 2003 SEM was

repeated using absorbed and bioavailable lead (instead of blood and total soil and dust lead levels), using SAS® software version 8 (SAS Institute Inc.). Several combinations of variables, including neighborhood soil means using radii of 200 ft, 500 ft, and 1,000 ft and age- and year-specific soil and dust categorical variables (i.e., grouped by both age and calendar year), were alternatively added, and model fit was evaluated by five criteria: *a*) convergence, *b*) chi-square probability test ($p > 0.05$), *c*) goodness of fit index (GFI) (> 0.90), *d*) parameters with significant t-statistics ($p < 0.05$), and *e*) parameter performance in subsequent IEUBK model analyses, described below (Carey 1998; SAS Institute Inc. 2008; Suhr 2006; Wothke 2010). Both the chi-square and GFI measure the difference between the expected and observed covariance matrices. Higher chi-square probability indicates better fit. The GFI ranges from 0 to 1.0, with higher values indicating better fit (Jöreskog and Sörbom 1988; SAS Institute Inc. 2008). SEM equations were solved using mean values for the independent variables and model parameters to estimate: *a*) soil and dust lead pathway parameters, *b*) neighborhood and community soil effects on lead uptake, *c*) age-specific and temporal effects in lead intake and uptake, and *d*) source partition scenarios for use in subsequent IEUBK modeling.

Ingestion Rate Estimates

Total lead uptake (µg/day) was calculated by dividing the measured BLLs (µg/dL) by the age-specific biokinetic slope factors, referred to as CR^{-1} (day/dL), used in the original IEUBK model (Harley and Kneip 1985; Jacobs Engineering et al. 1989; Kneip et al. 1983; TerraGraphics 1990, 2012; U.S. EPA 1994). Total lead uptake was partitioned into components used in the IEUBK model: air, diet, water, and soil/dust. Lead uptake from soil and dust was estimated by partitioned dust, yard soil, neighborhood soil (used only in the SEM), and community soil subcomponents by subtracting air, dietary, and drinking-water uptakes estimated from the IEUBK model default values (U.S. EPA 2001), as shown in Equation 2:

$$\begin{aligned} UP_{sd} = [&(C_d \times IR_d \times ABS_d) \\ &+ (C_{ys} \times IR_{ys} \times ABS_{ys}) \\ &+ (C_{cs} \times IR_{cs} \times ABS_{cs}) \\ &+ (C_{ns} \times IR_{ns} \times ABS_{ns})] \\ &= UP_{tot} - [UP_{air} + UP_{diet} + UP_{water}], \end{aligned} \quad [2]$$

where UP = lead uptake (µg/day); C = concentration (mg/kg); IR = ingestion rate (mg/day); ABS = absolute bioavailability (unitless); and (subscripts): sd = combined soil/dust sources; d = house dust; ys = yard soil; cs = community soil; ns = neighborhood soil (SEM); tot = total sources; air = airborne source; $diet$ = dietary source; $water$ = water source.

Equation 2 can be rearranged to calculate total soil/dust IRs [IR_{sd} (mg/day) is the sum of IR_d, IR_{ys}, IR_{cs}, and IR_{ns}] by assigning partition coefficients, i.e., fractional contributions to total soil/dust ingestion by each source, as follows in Equation 3:

$$\begin{aligned} IR_{sd} = 1{,}000 \times \{UP_{sd} / [&(C_d \times PT_d \times ABS_d) \\ &+ (C_{ys} \times PT_{ys} \times ABS_{ys}) \\ &+ (C_{cs} \times PT_{cs} \times ABS_{cs}) \\ &+ (C_{ns} \times PT_{ns} \times ABS_{ns})]\}, \end{aligned} \quad [3]$$

where PT = partition coefficient.

Partition coefficients used in these analyses included the IEUBK model default, those originally developed to support BHSS cleanup criteria, and values derived from SEM. Partition coefficients, resulting age-specific soil/dust IRs (using Equation 3), and bioavailability were input to the IEUBK model batch-mode analyses (IEUBKwin v1.1 build 11) to compare predicted and observed BLLs. The combined IR and partition scenarios showing best-predicted BLLs were evaluated by linear regression and sums of squared error (SSE). The slope nearest to 1.0 coupled with the highest r^2, highest F-statistic, and lowest sum of squared residuals from linear regression, as well as the SSE (squared difference between observed and predicted geometric mean BLLs), were used to determine the scenario(s) that best represent observed BLLs. The age-specific soil and dust IR estimates were then determined based on these scenario(s).

Results

Sample Analysis

The selected subset of historical data was considered generally representative of the parent database (e.g., lead concentration and child's age) (Table 1). The reanalyzed soil and dust lead concentrations were not significantly different

Table 1. Comparison of the parent BHSS database with the subset of records selected for reanalysis (historical data).

	Parent data set						Selected subset					
City	Minimum	Maximum	Average	SD	Geometric mean	Geometric SD	Minimum	Maximum	Average	SD	Geometric mean	Geometric SD
Kellogg	Parent data set $n = 3{,}054$						Selected subset $n = 118$					
Age (years)	0	9	5.1	2.7	—	—	1	9	5.5	2.6	—	—
Blood lead (µg/dL)	1	54	6.4	4.7	5.1	2.0	2	41	7.6	5.7	6.3	1.8
Soil lead (mg/kg)	100	13,400	954	1,625	274	4.4	100	6,930	1,407	1,849	435	5.2
Dust lead (mg/kg)	32	52,700	1,213	2,839	733	2.4	88	5,530	1,373	1,093	985	2.3
Page	Parent data set $n = 161$						Selected subset $n = 15$					
Age (years)	0	9	5.1	2.6	—	—	1	9	4.3	2.8	—	—
Blood lead (µg/dL)	1	26	7.0	4.7	5.7	1.9	3	12	5.6	2.4	5.2	1.5
Soil lead (mg/kg)	53	3,480	557	668	287	3.2	100	1,670	541	420	387	2.5
Dust lead (mg/kg)	69	2,070	678	496	478	2.6	86	1,680	706	567	467	2.9
Pinehurst	Parent data set $n = 1{,}369$						Selected subset $n = 117$					
Age (years)	0	9	5.1	2.6	—	—	1	9	5.2	2.4	—	—
Blood lead (µg/dL)	1	26	4.6	3.1	3.8	1.9	1	17	4.3	2.6	3.7	1.7
Soil lead (mg/kg)	31	3,060	438	424	312	2.3	37	1,700	469	356	369	2.0
Dust lead (mg/kg)	22	15,000	639	1,053	417	2.4	45	15,000	625	1,427	383	2.3
Smelterville	Parent data set $n = 642$						Selected subset $n = 57$					
Age (years)	0	9	4.9	2.7	—	—	1	9	4.5	2.6	—	—
Blood lead (µg/dL)	1	55	7.0	5.4	5.6	2.0	2	30	7.5	4.9	6.4	1.7
Soil lead (mg/kg)	100	10,700	953	1,921	245	4.3	100	8,170	1,037	1,821	242	4.8
Dust lead (mg/kg)	54	11,300	1,127	1,257	757	2.5	393	4,210	1,387	807	1,190	1.8
Wardner	Parent data set $n = 173$						Selected subset $n = 5$					
Age (years)	0	9	5.2	2.7	—	—	1	8	4.8	3.1	—	—
Blood lead (µg/dL)	1	20	6.6	3.8	5.5	1.9	2	8	4.6	2.2	4.2	1.6
Soil lead (mg/kg)	100	34,800	759	2,925	224	3.5	100	13,200	3,104	5,705	484	9.6
Dust lead (mg/kg)	130	6,000	1,005	1,112	700	2.3	307	2,220	1,147	697	959	2.1

from historical results (r^2 = 0.99, p < 0.01, n = 73; and r^2 = 0.91, p < 0.01, n = 193, respectively), indicating that samples were not compromised during storage. The reanalyzed sample results are summarized in Table 2. Mean soil bioavailability ranged from 30% to 39% by community, averaging 33% (SD ± 4%); dust bioavailability ranged from 27% to 30%, averaging 28% (SD ± 6%). Three "clean" soil samples were obtained in 2011 from borrow piles used to replace contaminated property soils. No clean yard soil samples were previously collected and archived. Consequently, these three samples represent postremediation replacement clean soils, and bioavailability results averaged 15% (SD ± 0.6%; data not shown). Linear regression relating soil and dust bioavailability to lead concentration showed a weak relationship (r^2 = 0.15, p = 0.0006 and r^2 = 0.045, p = 0.0028, respectively).

SEM Analyses

Several plausible SEM combinations met the model acceptance criteria. In each accepted model, bioavailable lead in dust and soils from the home yard, neighborhood, and community were all significant independent predictors of total blood lead uptake. Based on experience with the BHSS cleanup and development of the parent database, numerous combinations of spatial, temporal, and age-specific variable constructs and database time periods were explored (data not shown). Of the three neighborhood radii, 500 ft showed the best fit by combined chi-square test and parameter t-values. Age-specific coefficients for dust concentration among the youngest children (6 to < 24 months old) were significant (p < 0.01), implying different IRs, with a significant intercept representing uptake from other sources. Coefficients for age-specific and year-specific soil concentration variables were not significant (p > 0.05). The SEM with temporal variables showed marginally significant (p = 0.05) positive dust coefficients for 6- to 23-month-old children in 1994–1998, suggesting higher dust IRs during those years.

Source partitions using three SEM combinations were evaluated in subsequent IEUBK model analyses: Model 1 (1989–2002 database) included a term allowing calculation of year-specific IRs, and model 2 (1989–1998 database) and model 3 (1989–2002 database) assumed constant source contributions and IRs throughout each respective time period (Tables 3 and 4). Soil/dust IRs and source partitions were estimated by substitution of mean soil and dust lead concentrations in the model equations.

Model 2, shown in Equations 4 and 5 (chi-square test: p = 0.7416, n = 1,571; Table 3), was selected based on performance in subsequent IEUBK modeling:

$$\ln(UP_{tot}) = [0.1466 \times \ln(C_d \times ABS_d)] + [0.0516 \times \ln(C_{ys} \times ABS_{ys})] + [0.0440 \times \ln(C_d \times ABS_d \times \text{age0–1})] + [0.0613 \times \ln(C_d \times ABS_d \times \text{age1–2})] + [0.0661 \times \ln(C_{ns} \times ABS_{cs})] + [0.0954 \times \ln(C_{cs} \times ABS_{cs})] + 0.7666 \quad [4]$$

Table 2. Community averages of reanalyzed archived soil and house dust samples.

	Soil			Dust		
City	n	Soil lead (mg/kg) (mean ± SD)	Soil ABS (%) (mean ± SD)	n	Dust lead (mean ± SD) (mg/kg)	Dust ABS (%) (mean ± SD)
Kellogg	24	2,656 ± 1,624	34 ± 3	66	1,179 ± 934	28 ± 6
Page	7	778 ± 417	33 ± 4	12	753 ± 529	27 ± 5
Pinehurst	33	569 ± 463	32 ± 4	75	762 ± 2,131	28 ± 6
Smelterville	8	4,136 ± 2,192	39 ± 2	36	1,239 ± 550	30 ± 4
Wardner	1	2,030	30	4	892 ± 415	27 ± 5
Overall	73	1,686 ± 1,748	33 ± 4	193	996 ± 1,472	28 ± 6

ABS, absolute bioavailability.

Table 3. Structural equations modeling (SEM) results.

	Model 1 (1989–2002)			Model 2 (1989–1998)			Model 3 (1989–2002)		
Variables	Slope coefficient	t-Value[a]	Standardized coefficient	Slope coefficient	t-Value[a]	Standardized coefficient	Slope coefficient	t-Value[a]	Standardized coefficient
UP_{tot} (Equation 4)									
ln(UP_d)	0.1347	8.43	0.2575	0.1466	7.95	0.2762	0.1360	8.50	0.2598
ln(DUSTage0–1)	0.0450	2.80	0.0132	0.0440	2.24	0.0116	0.0450	2.79	0.0132
ln(DUSTage1–2)	0.0501	4.06	0.0273	0.0613	6.23	0.0333	0.0667	7.45	0.0363
ln(DUST1994–1998)	0.0336	1.95	0.0128	—	—	—	—	—	—
ln(UP_{ys})	0.0611	6.09	0.1027	0.0516	4.82	0.0866	0.0601	5.99	0.1010
ln(UP_{ns})	0.0647	3.30	0.1364	0.0661	2.41	0.1396	0.0636	3.24	0.1341
ln(UP_{cs})	0.1594	6.03	0.3439	0.0954	2.75	0.2050	0.1571	5.94	0.3389
Intercept	0.3639	3.34	0.1316	0.7666	5.55	0.2670	0.3820	3.52	0.1382
Error	—	—	0.2098	—	—	0.2021	—	—	0.2100
Bioavailable dust lead (Equation 5)									
ln(UP_{ys})	0.1039	7.57	0.0914	0.1054	7.31	0.0938	0.1039	7.57	0.0914
ln(UP_{ns})	0.0751	2.77	0.0828	0.1126	3.01	0.1262	0.0751	2.77	0.0828
ln(UP_{cs})	0.3350	9.35	0.3782	0.2582	5.50	0.2944	0.3350	9.35	0.3782
Intercept	2.3390	16.52	0.4418	2.5994	14.67	0.4804	2.3339	16.52	0.4418
Error	—	—	0.1523	—	—	0.1468	—	—	0.1523
Baseline bioavailable lead (µg/dL)	1.4			2.2			1.5		
Baseline bioavailable dust lead (mg/kg)	37.0			48.1			36.9		
n		2,034			1,571			2,034	
Goodness of fit index		0.9995			0.9999			0.9998	
χ^2		4.7284			0.598			1.5347	
Degrees of freedom		3			2			2	
Pr > χ^2		0.1928			0.7416			0.4642	
r^2 Total uptake		0.9560			0.9591			0.9559	
r^2 Bioavailable dust lead		0.9768			0.9785			0.9768	

Abbreviations: χ^2, chi-square; cs, community soil; d, dust; DUSTage0–1, bioavailable dust lead if the child was 6–11 months; DUSTage1–2, bioavailable dust lead if the child was 12–23 months; DUST1994–1998, bioavailable dust lead if the year was 1994, 1995, 1996, 1997, or 1998. ln, natural log; ns, neighborhood soil; Pr, probability; r^2, r-squared; tot, total; UP, uptake; ys, yard soil.
[a]t-Values ≥ 1.96 are equivalent to p-values < 0.05.

$$\ln(C_d \times ABS_d) = [0.1054 \times \ln(C_{ys} \times ABS_{ys})] + [0.1126 \times \ln(C_{ns} \times ABC_{cs})] + [0.2582 \times \ln(C_{cs} \times ABS_{cs})] + 2.5994, \quad [5]$$

where ln = natural log; C_{ns} = neighborhood soil arithmetic mean using 500-ft radius (mg/kg); age0–1 = 1 for 6–11 months, otherwise 0; age1–2 = 1 for 12–23 months, otherwise 0; ABS_{cs} applies to both C_{ns} and C_{cs} values.

The SEM standardized regression coefficients (Table 3) yielded partition coefficients of 50% house dust/25% yard soil/10% arithmetic mean neighborhood soil/15% arithmetic mean community soil (50/25/10/15) (Table 4) used in subsequent calculation of age-specific IRs.

Ingestion Rate Estimates

Figure 1 summarizes arithmetic and geometric mean soil/dust IRs calculated for four source partition scenarios: *a*) the IEUBK model default 55% dust/45% yard soil (55/45), *b*) the original BHSS model applying 40% dust/30% yard soil/30% geometric mean community soil (40/30/30G) (Panhandle District Health Department 1986), *c*) the same partition using arithmetic average community soil (40/30/30A), and *d*) the SEM (50/25/10/15). Calculated IRs were observed in three general ranges. The highest IR estimates were arithmetic means for the 55/45 partition and are near the IEUBK model recommended values (also shown in Figure 1). Mid- and low-range IR estimates are approximately one-third and one-half lower, respectively [corresponding numeric data with 95% confidence interval (CI) and percentiles are provided in Table S1].

IEUBK Model Results

The four IR and partition scenarios with the best agreement are from the mid-range IRs shown in Figure 1 (i.e., 40/30/30G-geometric mean IR (geoIR), 55/45-geoIR, 50/25/10/15-arithmetic mean IR (aveIR), 40/30/30A-aveIR; the high- and low-range IRs, respectively, over- and underpredicted observed BLLs (data not shown). Figure 2 shows the results of the SSE and linear regression analyses for annual observed and predicted geometric mean BLLs for the four scenarios with the best agreement. Observed geometric mean BLLs ranged from > 8 µg/dL in the late 1980s to near 2 µg/dL in 2002, and observed geometric standard deviations (GSDs) ranged from 1.52 to 2.12 (n = 2,176). GSDs calculated from the IEUBK batch runs for these four scenarios ranged from 1.42 to 2.10, with medians around 1.7 (see Table S2), consistent with the IEUBK model default GSD of 1.6.

Each of the four scenarios represents a plausible source partition and estimated lead intake scenario, produces similar IR estimates (Table 5), and shows temporal variability in the SSE, with the largest SSEs in 1988 (see Table S3). The scenarios with the smallest total SSE for 1989–2002 were 40/30/30G-geoIR, 55/45-geoIR, and 50/25/10/15-aveIR. The 40/30/30A-geoIR was similar to the 50/25/10/15-aveIR and had the next smallest SSE for those same years. Although all four scenarios showed temporal variation in predicting observed BLLs, the 50/25/10/15-aveIR had the lowest SSEs in the early and later years of the cleanup (1989–1990 and 1996–2002, respectively), whereas the 40/30/30G-geoIR had the lowest SSE in the middle years of the cleanup (1991–1995). Additionally, linear regression indicated that the 50/25/10/15-aveIR and the 40/30/30A-aveIR scenarios were best-fit models due to a slope coefficient nearest 1.0, in combination with highest r^2, largest F-statistic, and smallest sum of squared residuals (see

Table 4. Structural equations modeling (SEM) results for soil/dust contributions (%).

Variables	Model 1 (1989–2002) 0–2 years	Model 1 (1989–2002) 2–9 years	Model 1 (1989–2002) Value[a]	Model 2 (1989–1998) 0–2 years	Model 2 (1989–1998) 2–9 years	Model 2 (1989–1998) Value[a]	Model 3 (1989–2002) 0–2 years	Model 3 (1989–2002) 2–9 years	Model 3 (1989–2002) Value[a]
Contribution of dust/soil ingestion									
House dust	40	37	40	48	45	50	41	38	40
Yard	30	30	30	28	30	25	30	31	30
Neighborhood	11	11	10	9	10	10	11	11	10
Community	19	23	20	15	15	15	18	20	20
Contribution to lead in blood									
House dust			17			22			16
Yard			35			34			33
Neighborhood			14			15			14
Community			34			29			37

[a]Values are rounded to total 100%.

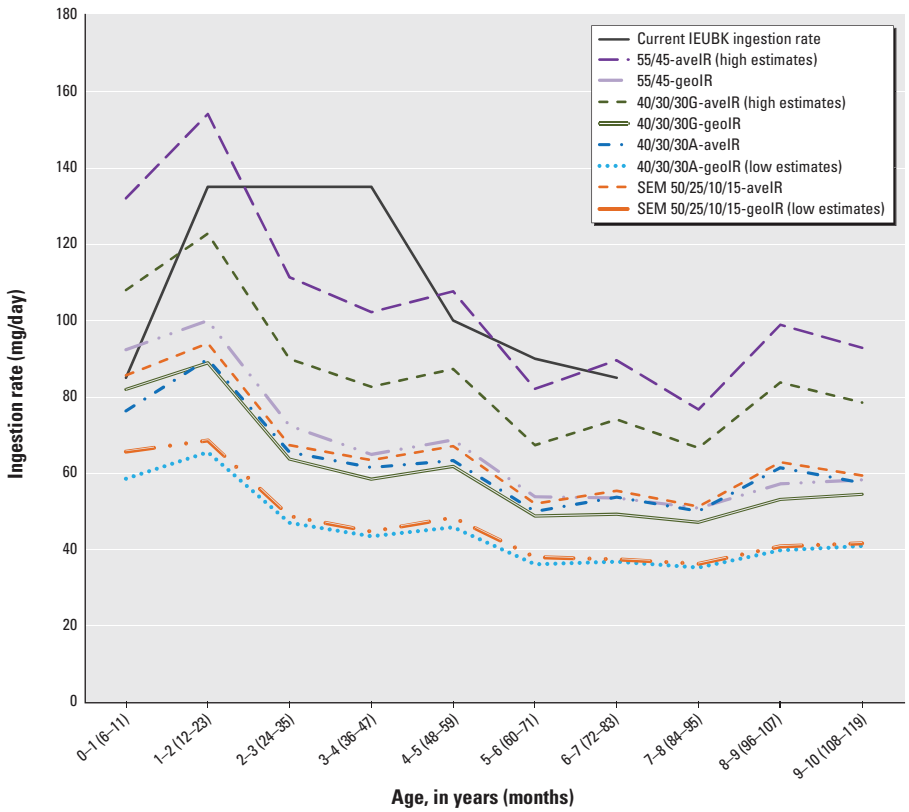

Figure 1. Arithmetic and geometric mean age-specific soil/dust ingestion rates (IRs) for four soil/dust partition scenarios. Included are current Integrated Exposure Uptake Biokinetic (IEUBK) model IRs and calculated age-specific mean soil/dust IRs for the four partition scenarios. For each age (6 months–9 years), arithmetic mean IRs (aveIR) and geometric mean IRs (geoIR) are shown. 55/45 is the partition of dust/yard soil, 40/30/30 is the partition of dust/yard/community soil, and SEM 50/25/10/15 is the partition of dust/yard/neighborhood/community soil. Corresponding numeric data, with 95% CI and percentile distributions for each model and age, are provided in Table S1.

Table S4). The age-specific IRs and 95% CIs for the 50/25/10/15-aveIR scenario are shown in Figure 3 because this scenario had the lowest SSEs in multiple years and was one of the best-fit linear regressions. Figure 3 also shows age-specific IRs recommended by U.S. EPA risk assessment guidance (U.S. EPA 1994, 2011).

Discussion

At the BHSS, children's soil/dust exposures have been investigated since the 1970s, and the IEUBK model has been used to evaluate the dose–response relationship since 1986. Use of the IEUBK model default IRs, bioavailability and soil/dust partition failed to account for soil sources beyond the immediate home yard and consistently overpredicted observed BLLs. In 1990, the BHSS cleanup criteria were developed using the 40/30/30G partition accounting for community soils and reduced soil/dust lead uptake (compared with the IEUBK model default). The overprediction of BLLs using default IEUBK model values was resolved by lowering soil and dust lead bioavailability, although it could have been explained by several combinations of reduced IRs or bioavailability. However at the time, it was not possible to determine which was predominant. In this study, we used a newly available laboratory method to estimate soil and house dust ABS. The soil and house dust bioavailability results of 33% and 28%, respectively, are similar to the recommended 30% IEUBK model default values and those found in other BHSS studies (Maddaloni et al. 1998). These findings suggest that IRs, not ABS, should be reduced by about 40% from the IEUBK default values to best represent the dose–response relationship observed at the BHSS.

In this study, the more rigorous SEM pathways analyses resulted in several plausible models, all suggesting that community and neighborhood soil sources, in addition to the yard soil source, are independent contributors to total lead uptake and bioavailable lead in house dust. Others have recently confirmed the importance of soil beyond the immediate home yard (Laidlaw et al. 2014; Zahran et al. 2013a, 2013b). The 50/25/10/15-aveIRs were derived from the only partition including neighborhood soils and exhibited the lowest SSEs in multiple years. These IRs were calculated using arithmetic-mean neighborhood and community soil exposures. The central tendency statistic that better approximates geographic area exposures has been the subject of debate and remains unresolved; the arithmetic mean represents an aggregate biased by high or low concentrations, and the geometric mean is the most likely concentration in the prescribed area. Two of the four select models employed arithmetic means, one used the geometric mean, and the IEUBK model default scenario uses individual observations and assumes the effect of soils beyond the home yard is included in house dust. However, all four models produced similar IRs with the average nearly identical to the 50/25/10/15-aveIRs, indicating the source partition is critical in describing lead intake.

Age-specific and temporal effects, also examined with SEM, suggested children 6–23 months of age exhibited greater lead intake rates from house dust than older children, consistent with the study by Wilson et al. (2013). Additionally, SEM analyses including year-specific variables suggested dust intake rates for younger children may have been lower early in the cleanup (1989–1993) and higher during the middle years of the cleanup (1994–1998). However, only age- and year-specific intake rates of interior dust were statistically significant predictors (Table 3); consequently, age- and year-specific IRs for soil intake (yard, neighborhood, or community) were not included in our final model (data not shown). Several factors may have caused temporal variations in IRs, or partition coefficients. Aggressive LHIP education and intervention programs may have resulted in a temporary reduction in soil/dust intake by children. Alternatively, elevated dust loadings caused by flooding and

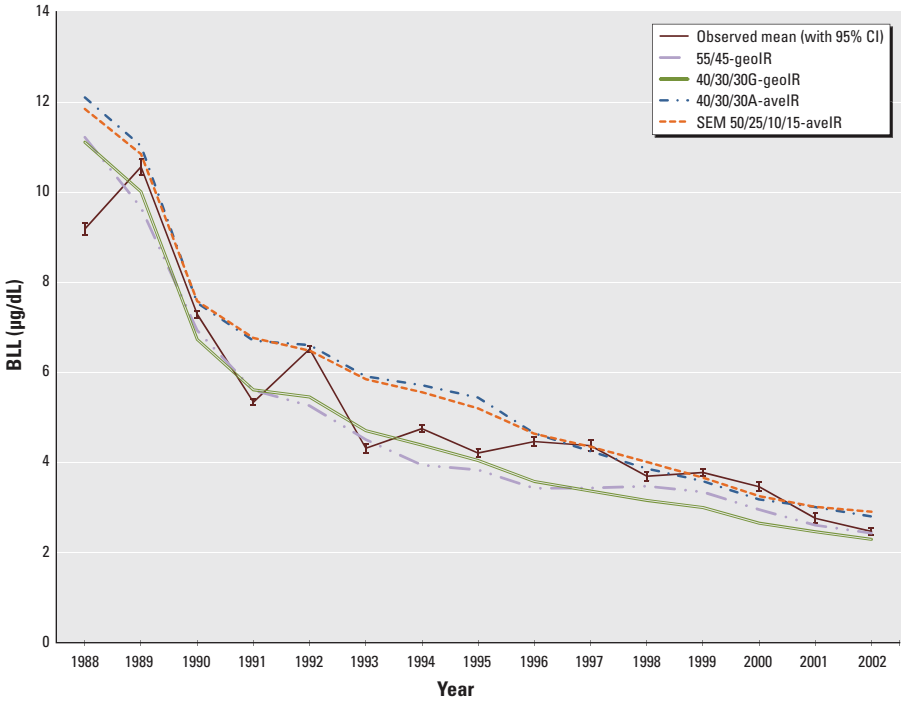

Figure 2. Observed and predicted geometric mean blood lead levels (BLLs) by year for four scenarios that best predict observed BLLs. Predicted geometric mean BLLs for the four scenarios are compared with observed BLLs from 1988 through 2002. Observed BLLs include error bars for the 95% confidence interval (CI). Abbreviations: aveIR, arithmetic mean ingestion rate; geoIR, geometric mean ingestion rate. 55/45 is the partition of dust/yard soil, 40/30/30 is the partition of dust/yard/community soil, and SEM 50/25/10/15 is the partition of dust/yard/neighborhood/community soil. Corresponding numeric data, with 95% CI and percentile distributions for each model and age, are provided in Table S1.

Table 5. Mean age-specific soil/dust ingestion rates (mg/day) for four scenarios that best predict observed blood lead levels.

Age[a] (years)	55/45[b]-geoIR	40/30/30G[c]-geoIR	40/30/30A[c]-aveIR	50/25/10/15[d]-aveIR	Average all models
0–1	92	82	76	86	84
1–2	100	89	90	94	93
2–3	72	64	66	67	67
3–4	65	58	62	63	62
4–5	69	62	63	67	65
5–6	54	49	50	52	51
6–7	54	49	54	55	53
7–8	51	47	50	51	50
8–9	57	53	61	63	59
9–10	58	54	57	59	57

Abbreviations: aveIR, arithmetic mean ingestion rate; geoIR, geometric mean ingestion rate.
[a]0–1 = 6–11 months, 1–2 = 12–23 months, 2–3 = 24–35 months, etc. [b]Dust/yard soil. [c]Dust/yard/community soil; G = geometric mean; A = arithmetic mean. [d]Dust/yard/neighborhood/community soil.

construction activities may have exacerbated ingestion in the middle years of the cleanup. However, SEM and IEUBK model sensitivity analyses investigating alternate time period (years) variable constructs suggested that variation in calculated IRs may be an artifact of the source partitions, nature of the data, or progression of the cleanup. At the beginning of the cleanup, there was little difference between community soil and neighborhood soil concentrations. As area-wide cleanups predominated, these variable concentrations diverged between 1994 and 1998 and returned to similar concentrations by 2000 (TerraGraphics 2004). The 50/25/10/15 SEM is the only partition scenario that captures spatial differentiation in soil outside the home yard through the neighborhood soil variable. It is also possible that various periods of the cleanup exhibited different partition ratios from landscape changes or LHIP activities.

The truncated 1989–1998 database was used to derive the select SEM partition because from 1999 forward, the yard, neighborhood, and community soil variables were dominated by remediated homes. Lead concentrations were not measured in remediated yards. Instead, a nominal value of 100 mg/kg was assigned to represent the maximum allowable recontamination level. Replacement soils, and presumably yard soil concentrations immediately following remediation, averaged ≤ 50 mg/kg (LFR Inc. 2008; McCulley, Frick & Gilman Inc. 1997). Consequently, remediated soil lead concentrations were likely biased high and reflected less variation in the final years of the cleanup. Including 1999–2002 in the SEM analyses could bias the standardized coefficients for soil lead parameters used to estimate source effects.

Additionally, SEM coefficients were based on 1,571 of 4,019 observations in the 1989–1998 database. Most missing variable measurements for the SEM subset were house dust lead levels, implying the home lacked a vacuum cleaner, and were associated with likely dustier homes and higher BLLs (TerraGraphics 2004; U.S. EPA 2000; von Lindern et al. 2003a, 2003b). As a result of the missing house dust levels, mean values for key variables in the SEM subset differ from those in the parent database; particularly, mean absorbed lead was about 11% greater for children with no dust lead observation. Because total absorbed lead was allocated to source variables, higher absorbed blood lead implies potentially higher soil/dust IRs, absorption rates, or dust lead concentrations, or a combination thereof among these underrepresented children. The LHIP provides free loaner high-efficiency particulate arresting vacuum cleaners to residents to address this need.

This study is part of larger cleanup and public health response. It was not a designed experiment. The LHIP paid participants a modest fee for blood and house dust samples specifically to identify and provide follow-up services to children at risk. Factors such as self-selection, repeat blood leads, uncontrolled vacuum dust samples, lack of a home vacuum cleaner, intervention responses, other lead sources, community awareness, and assumed clean soil values could bias the IRs higher or lower. Many of these factors were discussed in detail by von Lindern et al. (2003b).

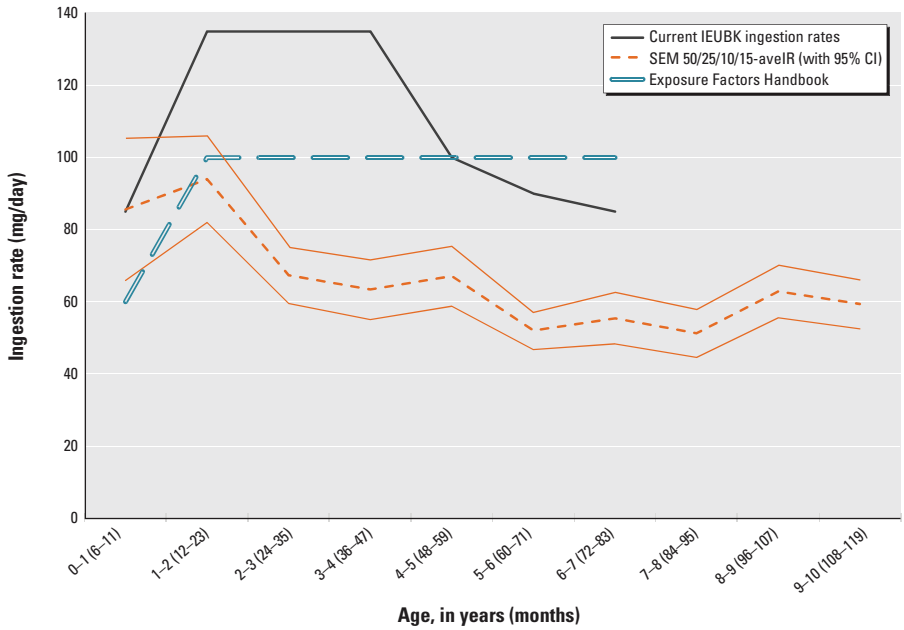

Figure 3. Mean age-specific ingestion rates (IRs) with 95% confidence intervals (CI) for the structural equations modeling (SEM) partition scenario. SEM 50/25/10/15 partition scenario (of dust/yard/neighborhood/community soil) with arithmetic mean IRs (aveIR) for ages 6 months–9 years, including 95% CI, are compared with current Integrated Exposure Uptake Biokinetic (IEUBK) model IRs and *Exposure Factors Handbook* IRs (ages 6 months–6 years only) (U.S. EPA 1994, 2011).

Conclusions

The addition of *in vitro* soil and house dust bioavailability estimates to the BHSS lead health database facilitated analysis of absorbed and bioavailable soil/dust lead, which improves understanding of the dose–response relationship and supports improved estimates of total soil/dust IRs. Bioavailability was substantially underestimated in the original BHSS risk assessment. The IEUBK model, using default bioavailability and default soil/dust IRs, consistently overpredicted BLLs collected from > 50% of resident children, and this was likely attributable to overestimating IRs. Although remediation activities were based on an inaccurate combination of IRs and bioavailability estimates, remediation was nonetheless effective in achieving the objective of < 5% of children with BLLs ≥ 10 µg/dL.

Soil and dust IRs at the BHSS from 1988 through 2002 averaged 66 mg/day (95% CI: 57, 75 mg/day) for children 6 months–9 years of age, and peaked at 94 mg/day (95% CI: 82, 106 mg/day) at age 12–23 months. The estimated IRs were lower than both IEUBK default and the U.S. EPA *Exposure Factors Handbook* recommended values for all ages except the youngest age group (< 12 months) (U.S. EPA 2001, 2011). The average IRs are 40% less than IEUBK default recommendations and 30% lower than estimates in the *Exposure Factors Handbook* (shown in Figure 3), and are consistent with recent studies and reviews suggesting values < 100 mg/day (Bierkens et al. 2011; Moya and Phillips 2014; Ozkaynak et al. 2011; Wilson et al. 2013).

Soil/dust IRs are among the most sensitive variables in the IEUBK and other risk assessment models used at hazardous waste sites (Griffin et al. 1999; TRW Lead Committee 2014). Accurately estimating lead intake requires simultaneously quantifying both soil/dust IRs and the soil/dust source partition. Inclusion of neighborhood and community soil exposures is essential to estimating soil/dust lead intake. These findings suggest that approximately half of the lead intake is from house dust and half is from soil, equally attributed to the immediate home yard and surrounding neighborhood/community. Additionally, the importance of soil outside the home environment varies with distance, not property boundaries, and intake estimates should account for soil sources in the immediate neighborhood and greater community.

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Exhibit K

ESTIMATION OF AGE-SPECIFIC SOIL AND DUST INGESTION RATES FOR U.S. CHILDREN: UPDATE TO THE DEFAULT VALUES FOR THE INTEGRATED EXPOSURE UPTAKE BIOKINETIC MODEL FOR LEAD IN U.S. CHILDREN

OVERVIEW

Since 1994, the Office of Land and Emergency Management (OLEM), formerly known as the Office of Solid Waste and Emergency Response (OSWER), has recommended the Integrated Exposure Uptake Biokinetic Model for Lead in Children (IEUBK model) as a risk assessment tool to support environmental cleanup decisions at current or future anticipated residential sites (U.S. EPA, 1994a, b). The IEUBK model predicts blood lead levels (PbB) in young children (birth to 7 years of age) exposed to lead from several sources and routes. The IEUBK model uses more than 100 input parameters that are initially set to default values. Of these, there are 46 parameters that may be input, or modified, by the user; the remainder are internal variables that are unavailable for modification (U.S. EPA, 1994a).

The IEUBK model uses empirical data from numerous studies of lead uptake and biokinetics, contact and intake rates of children with contaminated media, and data on the presence and behavior of environmental lead to predict a plausible distribution centered on the geometric mean (GM) of PbB for a hypothetical child or population of children (U.S. EPA, 2020).[1] The relative variability of PbB concentrations around the GM is defined as the geometric standard deviation (GSD). The GSD encompasses biological and behavioral differences, measurement variability from repeat sampling, variability as a result of sample locations and analytical variability.[2] From the distribution, the IEUBK model estimates the risk (*i.e.*, probability) that a child's or a population of children's PbB concentration will not exceed a certain PbB concentration (U.S. EPA, 1998, 1994a; White et al., 1998).

Ingestion of fine soil and dust particulates, especially by young children, is the dominant route of exposure for lead. (Laidlaw et al., 2014; Landrigan et al., 1975; Lanphear et al., 1998, 2003). Childhood soil and dust ingestion occurs via multiple pathways, including hand-to-mouth transfer, mouthing of objects, and contaminated food. The rate at which soil and dust is ingested are dependent on a child's age, individual behaviors, exposure time, total dust and soil accessible and environmental conditions (Zahran et al., 2013a,b). Age-specific estimates of the soil and dust ingestion rate pathway are needed to assess children's exposures in the home or play environment, and to make informed cleanup decisions.

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[1] The GM represents the central tendency estimate (*e.g.*, mean, 50th percentile) of PbB concentration of children from a hypothetical population (Hogan et al., 1998). If an arithmetic mean (or average) is used, the model provides a central point estimate for risk of an elevated PbB level. By definition a central tendency estimate is equally likely to over- or under-estimate the lead-intake at a contaminated site. Upper confidence limits (UCLs) can be used in the IEUBK model; however, the IEUBK model results could be interpreted as a more conservative estimate of the risk of an elevated PbB level. See U.S. EPA (1994a) for further information.

[2] The IEUBK model uses a log-normal probability distribution to characterize this variability (U.S. EPA, 1994a). The biokinetic component of the IEUBK model output provides a central estimate of blood lead concentration along with the distribution of possible blood lead concentrations in a population of similarly exposed children. In the IEUBK model, the GSD encompasses biological and behavioral differences, measurement variability from repeat sampling, variability as a result of sample locations, and analytical variability. The GSD is **not** intended to reflect variability in blood lead concentrations where different individuals are exposed to substantially **different** media concentrations of lead. The recommended default value for GSD (1.6) was derived from empirical studies with young children where both blood and environmental lead concentrations were measured (White et al., 1998).

The soil and dust ingestion rate is one of the most influential variables in the IEUBK model for lead in children (U.S. EPA, 1994a).

Early estimates of soil and dust ingestion rate in children were based on studies of trace elements in soil and feces (Battelle, 2005; Doyle et al., 2010; Sedman and Mahmood, 1994; U.S. EPA, 2011, 2012). The default values for the *Age-Dependent Soil and Dust Ingestion Rate* variable in the IEUBK model (v. 1.1, build 11) represent age-specific central tendency estimates for lead intake from soil and dust for children (6 to 84 months of age). The default values (v.1.1, build 11) are based on these tracer studies from a literature review and analysis performed during a review of the National Ambient Air Quality Standards (NAAQS) for lead (U.S. EPA, 1989, pp. A-16). The default soil and dust ingestion rate values are based on a study of soil ingestion in children (Sedman et al., 1989). This study utilized trace elements to quantify soil ingestion rates. The initial calibration of the IEUBK model employed these default values, and the results of a validation study performed in the early 1990s showed reasonably close agreement between model estimates using these intake values and empirical blood lead measurements (Hogan et al., 1998). The study that formed the basis for the existing default values did not, however, account for several factors that should be considered when designing a soil dust ingestion study (e.g., sieve to the currently recommended size fraction[3], sample household dust, soil outside of individual yards or the bioavailability of the lead in ingested soil or dust).

The purpose of this document is to provide the technical basis for an analysis of the currently available published literature to support an updated *Age-Dependent Soil and Dust Ingestion Rate (IRsd)* variable in the IEUBK model (Table 1). The updated age-specific soil and dust ingestion rate estimates for the *Age-Dependent Soil and Dust Ingestion Rate* variable in the IEUBK are based on soil and dust ingestion rates from scenario 3 of von Lindern et al. (2016). As described below in the Technical Analysis Section, this study was selected because it was determined that the approach employed by the authors provides the best central tendency estimate of age-specific soil and dust ingestion rates for use in the IEUBK to support risk assessments conducted under CERCLA or RCRA corrective action authority. The soil-dust ingestion rates from Scenario 3 results in soil-dust ingestion rates that are supported by other independent analyses that use dermal transfer to estimate soil and dust ingestion rate, specifically the modeled estimates from Ozkaynak et al. (2011) and Wilson et al. (2013) (see Table 2).

Soil/dust ingestion studies reviewed for this effort are not intended to specifically represent soil-dust ingestion for children who engage in pica behavior. The intake estimates for soil pica behavior would be greater than intake estimates for incidental ingestion of soil-dust, but reliable data for pica ingestion rates or frequency are not available[4].
The intended audience for this document is human health risk assessors familiar with using the IEUBK model in support of CERCLA and RCRA corrective action risk assessments. For further background information on both this variable and the use of the IEUBK model in Superfund lead risk assessment, refer to U.S. EPA (1994a) or the Technical Review Workgroup for Lead (TRW) website (https://www.epa.gov/superfund/lead-superfund-sites-guidance).

[3] Particle size should be similar to the fraction that adheres to skin to reflect the particles that are incidentally ingested during hand-to-mouth activity.
[4] See Chapter 5 of US EPA Exposure Factors Handbook for more information on pica.

Table 1. Recommended revision to default age-specific soil/ dust ingestion rates (mg/day) in the IEUBK model

Source	Age Category (months)							Basis for Age-Specific Value
	0<12	12<24	24<36	36<48	48<60	60<72	72<84	
IEUBK Model Default[a]	85	135	135	135	100	90	85	Methodology U.S. EPA, 1989 Data Source Sedman et al., 1989
Revised Soil/Dust Ingestion Rate	86	94	67	63	67	52	55	Methodology von Lindern et al., 2016 Ozkaynak et al., 2011 Wilson et al., 2013 Data Source von Lindern et al., 2016

[a]IEUBK model v. 1.1, build 11.

INTRODUCTION

The IEUBK model predicts PbB in young children (birth to 7 years of age) exposed to lead from several sources of exposure and routes. The IEUBK model uses more than 100 input parameters that are initially set to default values. Of these, there are 46 parameters that may be input, or modified, by the user; the remainder are locked (U.S. EPA, 1994a). Default values represent national averages or other central tendency values derived from empirical data in the open literature. Default values include a) lead concentrations in exposure media (*e.g.*, diet representative of national food sources); b) contact and intake rates (*e.g.*, soil/dust ingestion); and c) exposure durations (White et al., 1998). The representativeness of IEUBK model output is wholly dependent on the representativeness of the data (often assessed in terms of completeness, comparability, precision, and accuracy [U.S. EPA, 1994a]).

Representative site-specific data are essential for developing a risk assessment (as well as cleanup goals) that reflect the current or potential future conditions. The most common type of site-specific data is media-specific lead concentration information (air, water, soil, dust). Until recently, an inexpensive, validated method to estimate bioavailability of lead in soil or dust was not available. Receptor data (*e.g.*, age, body weight, breathing rate, or soil ingestion rate) does not typically vary from site to site.

To promote defensible and reproducible risk assessments and cleanup plans, while maintaining flexibility needed to respond to different site conditions, U.S. EPA recommends the Data Quality Objectives process (U.S. EPA, 2006). Data Quality Objectives provide a structured approach to collecting environmental data that will be sufficient to support decision-making (http://www.epa.gov/QUALITY/dqos.html).

TECHNICAL ANALYSIS

The initial default IEUBK total soil and dust ingestion rates were used in the development of the NAAQS (U.S. EPA, 1989). Rather than adding new data, many of the published studies since the initial default values were adopted in 1994 were reanalyzed data from previous studies. Moreover, the TRW identified a number of limitations of the re-analyses of the data that were published after 1994. For example, Stanek and Calabrese (2000) included estimates of daily soil ingestion that were significantly negative, biased by large negative values in the data. The decision to include the negative values and their consequent impact on the results was never addressed by the authors (Stifelman 2006). We have identified several newer and relevant studies on soil/dust ingestion from seven sources: Arnot et al., 2010; Bierkens and Cornelis, 2006; Jang et al., 2014; Ozkaynak et al., 2011; Stanek et al., 2012a,b; von Lindern et al., 2016; Wilson et al., 2013.

To evaluate these studies, the TRW Lead Committee used a data quality objective (DQO) approach (see Attachment 1). This approach (working through the first four steps of the DQO process) allowed the Committee to focus on identifying studies that provided information that would support a revision of the default age-specific soil-dust ingestion rates for use in the IEUBK model for assessing lead exposure at CERCLA and RCRA corrective action sites. Table 2 provides a summary of these literature sources.

The following studies were evaluated to support a revision to the soil and dust ingestion rate default parameter in the IEUBK. Arnot et al. (2010) described the Farfel Exposure Model (FHX) employed by Health Canada, which uses a soil/dust ingestion rate of 65 mg/day for children age 5-11 years, and 100 mg/day for toddlers (age 6-60 months). Bierkens and Cornelis (2006) derived a range of soil/dust ingestion values (23.2 to 116 mg/day assuming an 8-hour waking and outdoor period [alternate values for 12-hour waking and outdoor period shown in Table 2]) based on probabilistic modeling of other mouthing frequency and hand loading publications. A 4-day fecal study of Korean children age 0 to 84 months, using the limiting tracer method, calculated an arithmetic mean soil/dust ingestion rate of 118 mg/day and a geometric mean of 29.3 mg/day (Jang et al., 2014; tracer-specific data not provided in study). Ozkaynak et al. (2011) estimated a mean soil/dust ingestion rate for children 3 to 6 years of age (as compared to the age range of the IEUBK model which is children <72 months old) using stochastic human exposure and dose simulation (SHEDS) modeling, using activity diaries to estimate hand-to-mouth, and object-to-mouth contact rates. Stanek et al. (2012a,b) conducted a meta-analysis of their earlier four mass balance studies using stochastic modeling of the most reliable tracers of children from Amherst, Massachusetts; Anaconda, Montana; and Washington State. Soil pica data were excluded from their analysis. Soil/dust ingestion rates for children in specific age classes are shown in Table 2; an overall mean soil/dust ingestion rate of 25.5 mg/day (95^{th} percentile 79.4 mg/day) was estimated. Similar to Ozkaynak et al. (2011), Wilson et al. (2013) calculated soil and dust ingestion rates using a mechanistic model including parameters for particle loading on skin, transfer to hands, hand surface area, mouthing surface area, hand-to-mouth frequency, saliva dissolution, and exposure time using deterministic and probabilistic methods. Results, which are dependent on exposure time, were calculated separately for soil and dust, then summed for a daily soil/dust ingestion rate.

In addition, the information available on soil and dust ingestion rate values in EPA's Exposure Factors Handbook (U.S. EPA, 2017) was also considered as part of this effort but was not included in the peer review of this document (which preceded the release of the Exposure Factors Handbook update). The difference between the soil and dust ingestion rate values in the

Exposure Factors Handbook (U.S. EPA, 2017) and those proposed herein was addressed by the Office of Research and Development evaluation of the IEUBK model. (U.S. EPA, 2020).

The study by von Lindern et al. (2016) satisfies many of the evaluation criteria described in the TRW Lead Committee's DQOs (see Attachment 1). The authors of that study used environmental information collected at the Bunker Hill Mining and Metallurgical Complex Superfund Site (BHSS) site in Idaho to compare archived soil and dust samples from the BHSS to children's blood lead levels monitored from 1989 through 2002 to calculate soil/dust ingestion rates using the IEUBK model. Over 15 years of active cleanup, the Lead Health Intervention Program amassed approximately 5,400 blood lead observations (referred to as the parent database) from nearly 2,340 children (ages 0–9 and with a >50% participation rate) and yielding 2,176 records of blood/soil/dust lead concentrations. The study by von Lindern et al. (2016) used measured peak blood leads, community soil, neighborhood soil, yard soil concentration, house dust concentration and bioavailability information with IEUBK model defaults for Air, Water, and Diet to estimate soil-dust ingestion rates (IRs_D) under different Structural Equations Modeling (SEM) scenarios.

In the Bunker Hill study, four variables were used to quantify soil and dust exposures: house dust, yard soil, neighborhood soil (the mean of all yard soils within 200, 500, and 1000 feet of the home, excluding the home's yard), and community soil (the mean of all yard soils within the community, excluding the home's yard and neighborhood). The 271 samples (193 house dust samples, 73 yard soil samples and 5 quality control samples) were sieved to 80 mesh (to account for the particle size that would likely adhere to a child's hands) and analyzed for total lead and bioavailability.

The default assumption for the IEUBK model is that the source of soil ingested is 55% dust and 45% yard soil (U.S. EPA, 1994b). Structural Equations Modeling (SEM) was used to evaluate three different scenarios of yard soil to dust, neighborhood soil, and community soil:

1. 55% house dust/45% yard soil (as currently in the IEUBK model),
2. 40% house dust/30% yard soil/30% community soil, (alternatively using arithmetic or geometric means for community soil) and
3. 50% house dust/25% yard soil/10% neighborhood soil/15% community soil (alternatively using arithmetic or geometric means for neighborhood and community soil).

Table 2. Data summary of average soil/dust ingestion rates in children from selected studies.

Source	Soil/Dust Ingestion Rate (mg/day)	Age Range	n	Summary of Evaluation
IEUBK Model Default Values[a]	85-135	Children 0-84 months (yearly values)	77	Existing IEUBK model soil-dust ingestion rates Based on technical analysis to support the NAAQS for Lead (U.S. EPA, 1989).
Arnot et al., 2010	100	Children 6 60 months (age range)	n/a[b]	Is not considered a support document for revising the soil/dust ingestion rate because these are assumed input parameters for an exposure model using exposure factors for the general population of Canada. They are based on Health Canada 1998, which is based on Binder et al., (1986), Clausing et al. (1987), Calabrese et al. (1989), and Van Wijnen et al. (1990). Farfel Exposure Model (FHX) and Health Canada. 1998.[b]
	65	Children age 5 to 144 months (age range)		
Bierkens and Cornelis, 2006[c]	23.2-116	Children 12-84 months (age range) 8-hr awake and outdoors	5,000 (model runs)	Supportive study based on the limited number of observations.. Ranges of ingestion rates derived from probabilistic modeling of data from other publications reporting mouthing frequency and hand loading (Holmes et al., 1999; AuYeung et al., 2003; and U.S. EPA exposure factors, 2017).
	34.8-174	Children 12-84 months (age range) 12-hr awake and outdoors		
Ozkaynak et al., 2011	68	Children 36-72 months (age range) Mean value	1,000 (model runs)	Supportive study based on lack of new observation data. The estimates are based on modeling using SHEDS and hand-to-mouth and object-to-mouth contacts.
Jang et al., 2014	118	Children 0-96 months Arithmetic mean	58 samples	New tracer data based on Korean children. Estimates based on aluminum. The publication lacked details of the study. Only feces and soil-dust collected. 5 children were used as control group to compensate for exposure from other sources.
	29.3	Children 0-96 months Geometric mean	58 samples	

Source	Soil/Dust Ingestion Rate (mg/day)	Age Range	n	Summary of Evaluation
Stanek et al., 2012a,b	3.8	Children 12 to 36 months old	39 samples	Meta-analysis of four existing mass balance studies. The reanalysis of existing data is not a direct measurement and is not considered a candidate for supporting a revised default age-specific soil-dust ingestion rate
	20.6	Children 24 to 36 months old	55 samples	
	32.2	Children 36 to 60 months old	47 samples	
	40.9	Children 48 to 108 months old	75 samples	
U.S EPA Exposure Factors Handbook (2017)	40 - 90	Children < 6 months, 6 months to < 1, 1 to <2 years, 2 to <6 years, 1 to <6 years , 6 to < 12 years	241 in key tracer studies, 2,599 biokinetic modeling studies, modeled estimates of 1,000 simulated individuals and 200,000 trials.	The overall rating was low based on criteria of Soundness, Applicability and Utility, Clarity and Completeness, Variability and Uncertainty, and Evaluation and Review.
von Lindern et al., 2016	52-94[d]	Children 12 to 72 months old (yearly values)	985[f] (measured PbB and environmental values used for model runs)	Reanalysis of archived soil and dust data from Bunker Hill Superfund Site, available information includes bioavailability data, particle size and children's blood lead levels monitored (in some cases longitudinal data) from 1988-2002. Evaluated various combinations of dust, yard soil, neighborhood soil, and community soil. Accurately predicted peak annual blood lead from children representing greater than 50% of all resident children for 15 consecutive years.
Wilson et al., 2013	61	Toddlers 7 to 60 months	200,000 (model runs)	The study is considered a supportive study due to new modeled data. This study models soil/dust ingestion rates in Canada using hand-to-mouth transfer.
	55	Children 60 to 144 months		

[a]IEUBK model v. 1.1, build 11.
[b]Health Canada values based on data from Binder et al., 1986; Clausing et al., 1987; Calabrese et al., 1989; and Van Wijnen et al., 1990.
[c]Study reports values in units of mg/hr. The range (2.9-14.5 mg/hour) was converted to mg/d assuming both an 8-hour and a 12-hour waking and outdoor period.
[d]Results of Structural Equations Modeling (SEM) assuming 50% dust, 25% yard soil, 10% neighborhood soil, and 15% community soil.
[e] von Lindern et al. (2016) employed a hybrid approach that measured peak blood leads, particle size, community soil concentration, neighborhood soil concentration, yard soil concentration, as well as house dust concentration, and used IEUBK Modeled defaults for Air, Water, and Diet to estimate IRs under different SEM scenarios to select the model which best fit the empirical distribution of blood leads, representative of over 50% of the community for 15 consecutive years.
[f] 985 is the sum of 12-72 month old children in the 50/25/10/15 partition from Table S-1 of Supplemental Material to von Lindern et al. (2016).

The authors selected the model that provided the best fit to the empirical distribution of blood leads, which represented over 50% of the community for 15 consecutive years. Though ingestion rates for all three scenarios were similar, scenario 3 above had the lowest sum of squared error (SSE) in the statistical evaluation[5]. For this scenario, the authors derived age-specific, arithmetic mean soil/dust ingestion rates ranging from 52 to 94 mg/day for children age 1 to 6 years, with 95% confidence intervals ranging from 47 to 106 mg/day (Table 3). The other two scenarios were less acceptable because they did not fit the data as well.

Table 3. Soil/dust ingestion rates for the 50% house dust/25% yard soil/10% neighborhood soil/15% community soil scenario for the 12-71 month age range that is used in the IEUBK model (von Lindern et al., 2016).

Age[a]	n	AvgIR (95% CI)[b]	Percentiles						
			5	10	25	50	75	90	95
0-12	54	86 (66, 105)	17	27	38	72	94	165	221
13-24	174	94 (82, 106)	16	22	42	69	123	188	250
25-36	202	67 (59, 75)	10	19	28	53	82	140	178
37-48	209	63 (55, 72)	10	14	26	47	76	130	156
49-60	192	67 (59, 75)	11	15	32	53	86	122	182
61-72	208	52 (47, 57)	10	12	23	41	74	102	126
73-84	218	55 (48,62)	7	11	21	41	68	116	171

[a] Months
[b] AvgIR (95% CI) = arithmetic mean ingestion rate (95% confidence intervals)

After evaluating the available literature using the DQOs (see Attachment 1), the TRW Lead Committee recommends the age-specific soil-dust ingestion rates from scenario 3 of von Lindern et al. (2016) as the basis for revising the default age-specific soil-dust ingestion rates in the IEUBK model for CERCLA and RCRA corrective action risk assessments. As described above, this study was selected because it was determined that the approach employed by the authors most closely fits the DQOs established by the TRW Lead Committee for this effort; the study by von Lindern et al. (2016) provides the best estimate of age-specific soil and dust ingestion rates for use in the IEUBK model at CERCLA and RCRA 5,400 blood lead observations from nearly 2,340 individuals, yielding 2,176 records of blood/soil/dust lead concentrations over a 15 year timeframe with a >50% participation rate. In total, 271 samples (193 house dust samples, 73 yard soil samples and 5 quality control samples) sieved to 80 mesh (the particle size that adheres to a child's hand and most likely to be ingested by children) were analyzed for total lead and *in vitro* bioaccessibility. Community mean absolute bioavailability values (ABS) for unremediated yards soils and house dust, and site-wide ABS means for post-remediation soils were integrated into the database. Annual site-wide ABS means were calculated using a weighted average of bioavailable lead from remediated and unremediated yards. Aggressive LHIP education and intervention programs may have resulted in a temporary reduction in soil-dust intake rates by children, although this conclusion is not supported by multiple systematic reviews (Nussbaumer-Streit, Yeoh *et al.* 2016). Alternatively, elevated dust loadings caused by flooding and construction activities may have exacerbated soil-dust ingestion rates in the middle years of the BHSS cleanup. However, SEM and IEUBK model sensitivity analysis suggested that variation in calculated ingestion rates may be an artifact of the source partitions, nature of the data, or progression of the cleanup. The data collected at the BHSS best represents conditions at most CERCLA and RCRA corrective action sites during the Remedial

[5] Sum of Squared Error (SSE) is a statistical measure of the discrepancy between empirical values and the estimation model results. Lower SSE means better model prediction

Investigation and Feasibility Study phase of the remedial process. The soil-dust ingestion rates from Scenario 3 of von Lindern et al. (2016) results in soil-dust ingestion rates for the IEUBK model that are supported by other independent analyses, specifically the modeled estimates from Ozkaynak et al. (2011) and Wilson et al. (2013) (see Table 2).

UNCERTAINTY

Several studies published since 1994 were not applicable to this variable; for example, they contained only adult data, evaluated sediment ingestion rates rather than soil ingestion rates, or were review papers summarizing or reanalyzing other studies. Among recent publications that provide new data for young children (see Table 2), the TRW Lead Committee considered the study by von Lindern et al. (2016) to provide the relevant age-specific estimates of soil-dust ingestion rates for young children because it satisfied the most evaluation criteria (see Attachment 1) compared with the other studies. The TRW Lead Committee acknowledges that the data used by von Lindern et al. (2016) are site-specific and consideration was given to whether the Bunker Hill site was representative of other hazardous waste sites in the US. The data collected for that study were from an area of known lead contamination and could represent higher levels of lead than found in some areas. Also, as these data were collected from a site where EPA and other authorities were actively engaged in public outreach to reduce exposure, the soil-dust ingestion rates could be lower than in communities lacking public education efforts to limit exposure to soil and dust and thus may not necessarily be appropriate as an estimate for the general population, although the effectiveness of education has not been demonstrated in any of the Cochrane systematic reviews (Nussbaumer-Streit et al., 2016). Alternatively, elevated dust loadings caused by flooding and construction activities may have exacerbated soil-dust ingestion rates in the middle years of the BHSS cleanup. However, SEM and IEUBK model sensitivity analysis suggested that variation in calculated ingestion rates may be an artifact of the source partitions, nature of the data, or progression of the cleanup. The TRW Lead Committee notes that these conditions would likely occur at any CERCLA or RCRA corrective action site where USEPA was engaged in a risk assessment and therefore this limitation may be considered a strength (in that the data are possibly a better fit for the intended purpose than soil-dust ingestion rates collected from a naïve population would be). Furthermore, the information from this study is supported by two independent studies (Ozkaynak et al., 2011; Wilson et al., 2013). Thus, in the absence of other high-quality information the estimates from von Lindern et al. (2016) shown in table 3 are likely to be most representative of soil dust ingestion rates for young children at CERCLA and RCRA corrective action sites. The TRW Lead Committee did not, as part of this review process, define study acceptance criteria (aside from using the DQOs to guide the evaluation), conduct a systematic review, or conduct quality assurance activities on the published data to identify anomalies such as incorrect units, duplicate samples, etc. Consideration of additional studies published in the future could inform further refinement of age-specific soil and dust ingestion rates.

RECOMMENDATIONS FOR THE IEUBK MODEL

Results from several new studies provide information on average soil dust ingestion rates from children 0-84 months old. In general, these studies support an average combined soil/dust ingestion rate from 50 to 100 mg/day for children younger than 84 months old that could be applied to children residing near a CERCLA or RCRA corrective action site. For example, the two supporting studies Ozkaynak et al. (2011) and Wilson et al. (2013) result in values of 68 mg/day and 55-61 mg/day, respectively. These values are consistent with the recommended age-specific soil-dust ingestion rates for some of the similar age groupings from von Lindern et al.

(2016). The age-specific soil/dust ingestion recommended as the default soil/dust ingestion rates in the IEUBK model are shown in Table 4.

Table 4. Recommended change to soil/dust ingestion rates for use in the IEUBK model.

Age (years)	Age-specific, Average Soil/Dust Ingestion Rate (mg/day)	Basis for Age-Specific Value
0-1	86	Age-specific arithmetic mean ingestion rates based on the best fit model from von Lindern et al., 2016 and supported by modeled estimates from Ozkaynak et al., 2011; Wilson et al., 2013
1-2	94	
2-3	67	
3-4	63	
4-5	67	
5-6	52	
6-7	55	

Based on the evaluation described in this document and many factors specific to CERCLA and RCRA corrective action sites, these soil-dust ingestion rates are appropriate for assessing exposure at contaminated areas where the IEUBK model is frequently used. The TRW Lead Committee recommends updating the default *Age-Dependent Soil and Dust Ingestion Rate* variable in the IEUBK model to the age-specific average soil/dust ingestion rates based on von Lindern et al. (2016) (Table 3). These default values are considered appropriate for all applications of the IEUBK model where current and future residential scenarios are being assessed for CERCLA and RCRA corrective action risk assessment. The updated age-specific soil-dust ingestion rates are incorporated into the IEUBK model as shown in Figure 1.

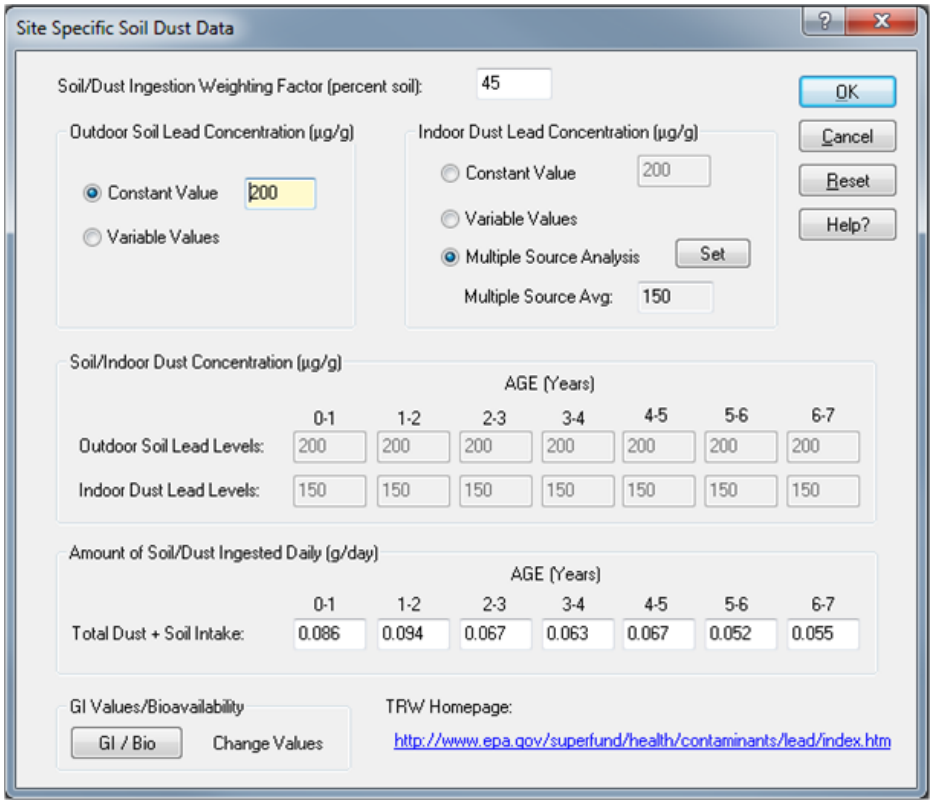

Figure 1. IEUBK Model Site Specific Soil Dust Data Entry Window with the Updated Soil/Dust Ingestion Rates.

IMPACT ON THE IEUBK MODEL PREDICTIONS

Using current IEUBK model (v.2) defaults for all parameters while implementing the proposed soil-dust rates will increase the preliminary remediation goal (PRG). Table 5 presents the updated estimates as well as the estimates from the previous analyses.

The PRGs in Table 5 are used to illustrate the impact when developing a screening level for lead in soil. As examples, the PRGs corresponding to PbBs of 10 µg/dL and 5 µg/dL are presented for illustrative purposes.

Table 5. Effects of changing the Soil-Dust Ingestion Rate (mg/day) in the IEUBK model

Study	Age Range	IRsd	P10 PRG[†]	P5 PRG[‡]
IEUBK Model (v1.1 build 11) default values	0-1 yr 1-2 yrs 2-3 yrs 3-4 yrs 4-5 yrs 5-6 yrs 6-7 yrs	85 mg/d 135 mg/d 135 mg/d 135 mg/d 100 mg/d 90 mg/d 85 mg/d	418 ppm	153 ppm
Proposed Update (based on von Lindern et al.	0-1 yr 1-2 yrs 2-3 yrs	86 mg/d 94 mg/d 67 mg/d	605 ppm	200 ppm

Study	Age Range	IRsd	P10 PRG[†]	P5 PRG[‡]
[2016]) using IEUBK v.2 default values	3-4 yrs 4-5 yrs 5-6 yrs 6-7 yrs	63 mg/d 67 mg/d 52 mg/d 55 mg/d		

[†] P10 PRG is the preliminary remediation goal for soil lead based on no more than 5% probability of exceeding a blood lead concentration of 10 µg/dL using IEUBK (v1.1. build 11) with default values for the 0-84 month age range.
[‡] P5 PRG is the preliminary remediation goal for soil lead based on no more than 5% probability of exceeding a blood lead concentration of 5 µg/dL using IEUBK (v1.1. build 11) with default values for the 0-84 month age range.

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ATTACHMENT 1. DATA QUALITY OBJECTIVES FOR THE SOIL-DUST INGESTION RATE LITERATURE EVALUATION

1. State the Problem
    a. Current IEUBK Model soil-dust ingestion rates do not reflect recent studies, which have addressed many of the problems of previous studies
        i. Age-specific rates
        ii. Dust rates
        iii. Confidence limits
        iv. Analytical uncertainty
            1. CV
            2. Negative values
        v. Study duration
            1. 5-20 days
        vi. Untested tracer bioavailability assumptions
        vii. Biomarkers
        viii. Sampling uncertainty
            1. Particle size
            2. Dust
            3. Exposure area
        ix. Number of subjects
        x. Transparency
            1. Stanek & Calabrese Data was not shared, despite requests & assurances
        xi. Consistency with other studies
            1. Multiple analyses of single datasets produce multiple estimates
        xii. Potential Conflict (or appearance) of interest
            1. PRP funding

2. Identify the Decisions
    a. IEUBK default
        i. Age-specific values
        ii. CTE values

3. Identify Inputs to the Decision
    a. Literature search
    b. Evaluation criteria
    c. Peer review

4. Define the Study Boundaries
    a. Timing
    b. Schedule
    c. Review process
    d. Impacts to programs & agencies

FMI see https://www.epa.gov/fedfac/guidance-systematic-planning-using-data-quality-objectives-process

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Exhibit L

Perpetua Resources Corp.
405 S. 8th Street, Ste 201
Boise, ID 83702
Tel: 208.901.3060
www.perpetuaresources.com

October 6, 2021

Kelli Wetzel
Permit Writer, Air Quality Division
Idaho Department of Environmental Quality
1410 North Hilton
Boise, ID 83706

Subject: **Facility ID No. 085-00011, Perpetua Resources Idaho, Inc., Stibnite Gold Project –TAP Addendum Report**

Dear Ms. Wetzel:

Perpetual Resources, Inc. is providing the enclosed TAP Addendum report (Addendum) for the Stibnite Gold Project. The Addendum contains the hazardous air pollutant (HAP) and toxic air pollutant (TAP) emissions calculations provided in the PTC application and as requested by IDEQ, supplements that information to support IDEQ's responses to comments.

If you have any questions regarding this submittal, please contact me at 208-901-3053 or alan.haslam@perpetua.us.

Thank you for reviewing this information.

Sincerely,
Perpetua Resources

Alan Haslam
Vice President – Permitting

Enclosure: TAP Addendum Report

AIR SCIENCES INC.

DENVER • PORTLAND • LOS ANGELES

Stibnite Gold Project Permit to Construct Application

TAP Addendum

Prepared For:
PERPETUA RESOURCES IDAHO, INC.

PROJECT NO. 335-21-404
OCTOBER 5, 2021

TABLE OF CONTENTS

Tables

Figures

Appendices

1.0 INTRODUCTION

On September 10, 2020 and February 18, 2021, the Idaho Department of Environmental Quality (IDEQ) provided notices for public comment on the Perpetua Resources Idaho, Inc. (hereafter referred to as Perpetua Resources) Stibnite Gold Project (SGP) complete application materials (Application), draft permit to construct (Draft PTC), and statement of basis (SOB). The public comments received included requests for additional information regarding hazardous air pollutant (HAP) and toxic air pollutant (TAP) emission estimates and modeling.

The purpose of this TAP Addendum (Addendum) is to provide that additional information to support IDEQ's responses to comments. The information provided in this Addendum confirms the following determinations made by Perpetua Resources and IDEQ at the time of the public notices:

1. The SGP is an area source for HAP emissions.

2. The SGP complies with the Idaho TAP provisions (IDAPA 58.01.01.210).

3. The SGP complies with the Idaho mercury rule (IDAPA 58.01.01.215).

This Addendum supplements information in the complete Application and supports those determinations highlighted during the public comment. Section 2.0 provides a description of the HAP/TAP emission calculations and source status. Section 3.0 provides a TAP emissions evaluation and modeling analysis, including TAP emission sources covered by IDAPA 58.01.01.210.20. Section 4.0 compares arsenic modeling analyses for actual and potential arsenic emissions. Section 5.0 provides a discussion of the emission reductions that demonstrate compliance with carcinogenic TAPs. Section 6.0 provides a Toxic Air Pollutant Reasonably Available Control Technology (T-RACT) analysis. Section 7.0 provides proposed permit conditions for demonstrating compliance with carcinogenic TAPs, and Section 8.0 provides a discussion of mercury emissions, including mercury emission sources covered by IDAPA 58.01.01.215.01.

IDAPA 58.01.01.210 and 215 reduce the information required from a PTC applicant and streamline the PTC review required by IDEQ in those circumstances where the HAP/TAP emissions are covered or addressed by federal regulations (IDAPA 58.01.01.210) or the mercury emissions are below a specific exemption threshold (IDAPA 58.01.01.215). Perpetua Resources referenced these rules in the Application and relied on these provisions to present a complete HAP/TAP emissions inventory that aligned with these rules. To support IDEQ's responses to public comments, IDEQ requested that Perpetua Resources expand its HAP/TAP analyses beyond the requirements of these rules and reconfirm compliance with TAP thresholds. This additional work reconfirms IDEQ's earlier findings that the SGP is an area source, and the proposed HAP/TAP emissions comply with IDAPA 58.01.01.210 and 215.

2.0 HAP/TAP EMISSIONS

During the two IDEQ public comment periods, IDEQ received comments regarding the following:

1. SGP source status for HAPs
2. Metal HAP/TAP emissions from fugitive dust
3. Metal HAP/TAP emissions from the autoclave and lime kiln processes
4. Fugitive emissions of hydrogen cyanide (HCN)

To support IDEQ's responses to comments and confirm the SGP area source status, the potential-to-emit (PTE)[1] HAP/TAP emission inventory in Appendix A of this Addendum contains emission calculations for all HAPs and TAPs emitted from all the SGP processes, including:

- Metals from mining fugitive dust emissions
- Metals from ore processing, ore concentration and refining, and lime, aggregate, and concrete production
- Antimony (Sb) emissions from the Sb drying and bagging circuit
- Sulfuric acid (H_2SO_4) and hydrogen sulfide (H_2S) from the autoclave, and hydrochloric acid (HCl) emissions and lime kiln
- Evaporative HCN from cyanide leaching and the tailings storage facility
- Various HAPs/TAPs from fuel storage and combustion
- Carbon disulfide emissions from the use of xanthate
- Evaporative mercury from mining surfaces

This HAP/TAP emission inventory was conducted for all 14 modeling scenarios evaluated in the Application. The emissions provided in Appendix A reflect the highest emissions scenario (HAP/TAP Emission Calculations – Scenario W3, 180,000 T/day).[2]

[1] PTE in this Addendum refers to the potential emissions after applying all proposed *air pollution control equipment and restrictions on hours of operation or on the type or amount of material combusted, stored or processed* per IDAPA 58.01.01.006.88 (i.e., PTE is the proposed permitted emissions).

[2] HAP/TAP Emission Calculations – Scenario W3, 180,000 T/day: HAP/TAP emissions based on the potential mining production rate of 180,000 tons per day (T/day) and the highest emissions scenario (Modeling Scenario W3).

2.1 Description of HAP Source Status

2.1.1 Controlled HAP Emissions

The controlled HAP emissions (PTE) from the SGP are below the major source thresholds; therefore, the SOB classified the SGP as an area source for HAP emissions. This is consistent with EPA's determination that all U.S. gold mine ore processing and production facilities are area sources.[3] The emissions inventory provided in Appendix A shows the total HAP emissions are 3.67 tons per year (ton/yr) for a single HAP and 12.56 ton/yr for all the HAPs combined for the highest emissions scenario (Modeling Scenario W3). The major source levels are 10 ton/yr for a single HAP and/or 25 ton/yr for all the HAPs combined.

2.1.2 Uncontrolled HAP Emissions

Uncontrolled HAP emissions are estimated to exceed 25 ton/yr, combined; therefore, to support the area source designation, Perpetua Resources committed to operational limitations and emission controls in the Application that achieve area source status.

2.2 Description of HAP/TAP Emission Calculations

This section provides a brief description of the methods used to calculate the HAP/TAP emissions provided in Appendix A. The references used for the HAP/TAP calculations were presented in the Application. Any new references are provided in this section.

2.2.1 Metal Emissions from Mining Fugitive Dust

The metal HAP/TAP emissions from fugitive dust generated by mining activities (drilling, blasting, excavating, hauling, etc.) were calculated by multiplying the HAP/TAP-specific median metal concentration in the ore[4] by the activity-specific total particulate matter (PM) emissions. The median metal concentrations were derived from over 55,000 core samples taken primarily from the more mineralized zones of the SGP pits (i.e., in and around gold ore deposits).

This emissions inventory does not reflect any of the emission reductions described in Section 5.0 for carcinogenic TAP compliance.

[3] *EPA recently gathered data and evaluated emissions of other HAP, including cyanide and non-mercury metals. The data indicate that the gold mining processing and production category consists of only area sources (i.e., facilities that emit less than ten tons per year of any one HAP and less than 25 tons per year of any combination of HAP)* (EPA 2010).

[4] Iron (Fe) and selenium (Se) were not included in the Application because the concentrations of these metals were similar to typical crustal abundance levels. In response to comments on HAPs/TAPs emissions, the concentrations of these metals (18,200 ppm of Fe and 0.4 ppm of Se) are provided (Midas Gold 2020).

2.2.2 Metal Emissions from Ore Processing and Lime/Aggregate Production

2.2.2.1 Crushing, Screening, and Material Handling

The metal HAP/TAP emissions generated by process and production sources (the crushing, screening, and handling of ore, limestone, lime, and aggregate) were calculated by multiplying the PM emissions from these sources by the median concentration of metals in the ore, limestone, lime, or aggregate. The ore median metal concentrations are discussed in Section 2.2.1. The limestone, lime, and aggregate metal concentrations are provided in Table 1.

The limestone metal concentrations were measured from core hole samples through the middle marble formation in the proposed limestone quarry's footprint. These rock samples were specifically analyzed to assess the formation as a viable limestone source. As a conservative estimate, the limestone metal profile was also used for aggregate production.

Table 1. Metal TAP Concentrations for Limestone and Lime

CAS	TAP Name	Concentration (ppm) [1]
7440-38-2	Arsenic	23
7440-41-7	Beryllium	0.8
7440-43-9	Cadmium	0.25
7440-48-4	Cobalt	4
7440-47-3	Chromium	15
7439-97-6	Mercury	0.02
7439-96-5	Manganese	236.5
7440-02-0	Nickel	5
7439-92-1	Lead	3
7440-36-0	Antimony	2.5
7723-14-0	Phosphorus	130
7440-22-4	Silver	0
7429-90-5	Aluminum	22,600
7440-39-3	Barium	145
1317-65-3	Calcium Carbonate [2]	274,500
1305-78-8	Calcium Oxide [3]	740,000
7440-50-8	Copper	5
7439-89-6	Iron	10,350
7439-98-7	Molybdenum	0.5
7440-28-0	Thallium	5
7440-61-1	Uranium	5

CAS	TAP Name	Concentration (ppm) [1]
7440-62-2	Vanadium	15.5
7440-33-7	Tungsten	5
7440-66-6	Zinc	18

[1] Median of 98 samples of the SGP limestone material (M3 2018).
[2] Calcium carbonate ($CaCO_3$) is used for limestone processing.
[3] Calcium oxide (CaO) is used for lime processing. 40% to 74% CaO (NLA 2007).

2.2.2.2 Lime Kiln

The non-mercury metal HAP/TAP emissions from the lime kiln were calculated by multiplying the PM emissions by the median concentration of metals in the limestone shown in Table 1. The mercury emissions from the lime kiln were conservatively estimated by assuming all mercury in the limestone feed is volatilized and emitted.

2.2.2.3 Autoclave

Mercury emissions from the SGP autoclave were based on the SysCAD modeling of the SGP autoclave performed by Perpetua Resources' engineering contractor: M3 Engineering. This modeling predicted 0.0105 grams per second of mercury emissions exiting the autoclave mercury control system, which is comprised of a venturi scrubber, a vent gas cleaning tower, a vent gas steam condensation tower, and one or more sulfur-impregnated activated carbon filters.

The non-mercury metal HAP/TAP emissions from the autoclave mercury control system are expected to be less than the mercury emissions because non-mercury HAP/TAP emissions are only particulates and more easily controlled by the emissions control system. Mercury emissions move through the control system as both particulate and gas. For this review, the non-mercury HAP/TAP emissions were conservatively assumed to be equal to the mercury emissions.

2.2.2.4 EW Cells, Pregnant Solution Tank, Retort, Furnace, and Carbon Kiln

Mercury emissions from the SGP electrowinning (EW) cells, pregnant solution tank, mercury retort, induction melting furnace, and carbon regeneration kiln were calculated based on stack test data from similar sources utilizing similar mercury control systems at Nevada gold mines.

The non-mercury metal HAP/TAP emissions exiting these mercury control systems are expected to be less than the mercury emissions because non-mercury HAP/TAP emissions are only particulates and more easily controlled by the emissions control system. Mercury emissions move through the control system as both particulate and gas. For this review, the non-mercury HAP/TAP emissions were conservatively assumed to be equal to the respective mercury emissions.

2.2.2.5 Antimony Dryer and Dry Bagging

The Sb circuit proposed in the Application was replaced with a new dewatering/packaging circuit. The new circuit eliminates the potential for metal emissions from dust and mercury evaporation emissions from concentrate heating. Instead, the Sb concentrate will be dewatered using a filter press and then bagged as a wet (damp) product. There are no HAP/TAP emissions associated with this new circuit.

2.2.3 Metal Emissions from Concrete Production

The metal HAP/TAP emissions from concrete production were calculated using EPA emission factors from AP-42 Section 11.12, Concrete Batching. This section provides controlled emission factors for cement silo filling and central mix batching. There are no emission factors for cement silo unloading. Therefore, the cement silo filling factors were used for cement silo unloading as a conservative estimate.

Chromium (VI) percentages of the total chromium were provided by IDEQ for cement silo filling and central mix batching. These percentages were used to calculate chromium (VI) emissions from cement silo filling and unloading and central mix batching.

There are no HAP/TAP emission factors for the dust generated from aggregate handling in the concrete production process. As a conservative estimate, the limestone metals profile provided in Table 1 of Section 2.2.2.1 was used to estimate the HAP/TAP emissions from aggregate handling.

2.2.4 H_2SO_4 and H_2S Emissions from the Autoclave

H_2SO_4 and H_2S emissions from the SGP autoclave were calculated based on source test data from similar autoclaves at gold mines in Nevada.

2.2.5 HCl Emissions from the Lime Kiln

The HCl emissions from the lime kiln were calculated using the HCl emission factor obtained from EPA's EPCRA Section 313 Guidance for Reporting Hydrochloric Acid (EPA 1999b).

2.2.6 HCN Emissions from Cyanide Leaching and Tailings Storage Facility

The evaporative HCN emissions from cyanide leaching and the tailings storage facility were calculated using the flux methodology developed by EPA and the Nevada Mining Association as part of the 40 CFR 63 rule-making process. The methodology is based on empirical measurements at several gold mines in Nevada taken under the direction of EPA. Numerous gold mines in several states have used this method since its development in 2010.

2.2.7 HAP/TAP Emissions from Fuel Storage and Fuel Combustion

HAP/TAP emissions from fuel combustion (propane and diesel) were calculated using fuel combustion rates and the applicable EPA AP-42 emission factors.

HAP/TAP emissions from fuel storage (gasoline) were calculated from the tank volatile organic compound (VOC) emissions multiplied by the weight percentages of HAP/TAP in the fuel. The percentages were obtained from EPA's EPCRA Section 313 Industry Guidance Metal Mining Facilities, Table 3-8 for gasoline (EPA 1999a).

2.2.8 Carbon Disulfide Emissions from Xanthate

Carbon disulfide (CS_2) emissions from potassium amyl xanthate (PAX) use were calculated based on the decomposition of xanthate to CS_2 gas. The decomposition rate was determined from published experimental data.

2.2.9 Evaporative Mercury Emissions from Mining Surfaces

Mercury can evaporate from rock surfaces in pits, tailings facilities, development rock storage facilities, and stockpiles. The rate of mercury evaporation (or flux) is a function of the mercury concentration in the material. Mercury flux rates and concentration measurements taken at a gold mine in Nevada were adjusted for the SGP mercury concentrations to estimate mercury flux emissions from the SGP pits, tailings facility, development rock storage facilities, and ore stockpiles.

3.0 TAP ANALYSIS

A complete inventory of the PTE TAP emissions is provided in Appendix A, as discussed in Section 2.0. Appendix A also identifies the applicability of IDAPA 58.01.01.210.20. According to IDAPA 58.01.01.210.20, no further demonstration of compliance with the TAP provisions is required to obtain a PTC for new source emissions, such as the SGP, from:

a. The equipment or activities covered by a New Source Performance Standards (NSPS) or National Emissions Standards for Hazardous Air Pollutants (NESHAP); or

b. The source category of equipment or activities addressed by a NSPS or NESHAP even if the specific equipment or activity is not subject to compliance requirements under the federal rule.

After applying IDAPA 58.01.01.210.20 as described in Section 3.1, the remaining TAP emissions are subject to further compliance demonstration and are compared to the screening emission levels (EL) described in Section 3.3. TAP emissions that below the screening EL, require no further demonstration of compliance with the TAP provisions. TAP emissions above the screening EL require modeling, as described in Section 3.4. To identify the TAPs subject to review, Section 3.2 provides a comparison of the metals analyzed in the SGP ore, development rock, and limestone to the TAPs listed in IDAPA 58.01.01.585 and IDAPA 58.01.01.586.

3.1 Equipment or Activities Covered or Addressed by NESHAP or NSPS

In accordance with IDAPA 58.01.01.210.20, the equipment and activities at the SGP that are either covered or addressed by NESHAP or NSPS are discussed in the following subsections. TAPs emitted from these sources that are also HAPs require no further evaluation to demonstrate compliance with the TAP provisions. TAP emissions from these sources that are not HAPs require additional review to demonstrate compliance with the TAP provisions.

3.1.1 NESHAP Subpart ZZZZ

40 CFR 63, Subpart ZZZZ, NESHAP for Stationary Reciprocating Internal Combustion Engines covers HAP emissions from the SGP emergency generators and fire pump (Source ID No. EDG1, EDG2, EDG3, and EDFP). IDAPA 58.01.01.210.20(a) applies to Source ID No. EDG1, EDG2, EDG3, and EDFP.

3.1.2 NESHAP Subpart AAAAA

40 CFR 63, Subpart AAAAA, NESHAP for Lime Manufacturing Plants addresses HAP emissions from the SGP lime manufacturing sources (Source ID No. LS12, LK, LS-L/U, LCR, and LKC).[5] IDAPA 58.01.01.210.20(b) applies to Source ID No. LS12, LK, LS-L/U, LCR, and LKC.

3.1.3 NESHAP Subpart CCCCCC

40 CFR 63, Subpart CCCCCC, NESHAP for Source Category: Gasoline Dispensing Facilities covers the SGP gasoline storage tanks (Source ID No. TG1 and TG2). IDAPA 58.01.01.210.20(a) applies to Source ID No. TG1 and TG2.

3.1.4 NESHAP Subpart EEEEEEE

40 CFR 63, Subpart EEEEEEE, NESHAP: Gold Mine Ore Processing and Production Area Source Category covers HAP emissions from the SGP autoclave (Source ID No. AC) and the EW cells, pregnant solution tank, mercury retort, induction melting furnace, and carbon regeneration kiln (Source ID No. EW, MR, MF, and CKD). IDAPA 58.01.01.210.20(a) applies to Source ID No. AC, EW, MR, MF, and CKD.

The NESHAP source category addresses HAP emissions from mining activities, specifically fugitive dust-generating activities (drilling, blasting, excavating, hauling, etc.), explosives use and storage (Source ID No. PS), cyanide leaching (Source ID No. CIP Leach 1-4, CIL 1-6, CIP 1-6, and CN Detox 1-2), tailings storage, ore processing (Source ID No. OC1-13), ore processing heating (Source ID No. ACB, CKB, PV, and HS), and the ore processing reagent use of PAX and sodium cyanide (NaCN). The NESHAP source category is defined as "*Gold Ore Mining ..., NAICS code 212221, Establishments primarily engaged in developing the mine site, mining, and/or beneficiating (i.e., preparing) ores valued chiefly for their gold content. Establishments primarily engaged in transformation of the gold into bullion or doré bar in combination with mining activities are included in this industry*" (EPA 2011b). EPA's rule-making docket (Docket ID EPA-HQ-OAR-2010-0239) provides documents evaluating HAP metal emissions from mining fugitive dust, HCN emissions from cyanide leaching, and downwind HCN ambient concentrations.[6]

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[5] NESHAP Subpart AAAAA defines the affected source as follows: *each lime kiln and its associated cooler, each individual PSH [processed stone handling] system. The individual types of emission units in a PSH system are conveying system transfer points, bulk loading or unloading systems, screening operations, bucket elevators, and belt conveyors-if they follow the processed stone storage bin or storage pile in the sequence of PSH operations. The materials processing operations (MPO) associated with lime products (such as quicklime and hydrated lime), lime kiln dust handling, quarry or mining operations, limestone sizing operations, and fuels are not subject to today's final NESHAP. Processed stone handling operations are further distinguished in the final NESHAP as follows: (1) whether their emissions are vented through a stack, (2) whether their emissions are fugitive emissions, (3) whether their emissions are vented through a stack with some fugitive emissions from the partial enclosure, and/or (4) whether the source is enclosed in a building* (69 Fed. Reg. 394, 397 (January 5, 2004)).

[6] EPA-HQ-OAR-2010-0239-0132, *Profile of the Metal Mining Industry;* EPA-HQ-OAR-2010-0239-0157, *Recommended Methodology for Quantification of Fugitive Dust Metals Emissions from Mining Activities for Title V Applicability;* EPA-HQ-OAR-2010-0239-0102, *QAPP Comprehensive Air Emissions Testing for Hydrogen Cyanide;* EPA-HQ-OAR-2010-0239-0134, -0135 -0136 -0137 -0161 -0162 -0378, *Meteorological and Hydrogen Cyanide (HCN) Fence Line Monitoring* reports.

In response to public comments, this Addendum applies IDAPA 58.01.01.210.20(a) to those sources of HAP emissions at the SGP that are covered by Subpart EEEEEEE. This Addendum provides further evaluation of the sources of HAP emissions that are addressed by the NESHAP per IDAPA 58.01.01.210.20(b) – the mining emissions.[7]

3.1.5 NSPS Subpart LL

40 CFR 60, Subpart LL, Standards of Performance for Metallic Mineral Processing Plant covers the SGP ore processing (Source ID No. OC1-13). IDAPA 58.01.01.210.20(a) applies to Source ID No. OC1-13.

3.1.6 NSPS Subpart OOO

40 CFR 60, Subpart OOO, Standards of Performance for Nonmetallic Mineral Processing Plants covers the SGP limestone processing sources (Source ID LS1-11 and LSBM), aggregate production (Source ID No. PCSP1 and PCSP2), and aggregate handling in the concrete production process (Source ID No. CA-L/U). IDAPA 58.01.01.210.20(a) applies to Source ID No. LS1-11, LSBM, PCSP1, PCSP2, CA-L/U.

3.2 Metals Review for TAP Provisions Applicability

Table 2 provides a comparison of the metals analyzed in the SGP ore, development rock, and limestone to the TAPs listed in IDAPA 58.01.01.585 and IDAPA 58.01.01.586.

Table 2. Metals Comparison to IDAPA 58.01.01.585-586 TAPs

Metal			TAP		
CAS	**Name**	**HAP?**	**CAS**	**Name**	**Is the Metal a TAP?**
7440-57-5	Gold	No	7440-57-5	Not listed	No
7440-22-4	Silver	No	7440-22-4	Silver - Including metal soluble compounds, as Ag	Yes, same CAS Yes, similar form No
7429-90-5	Aluminum	No	7429-90-5	Aluminum, including: Metal & Oxide Pyro powders Soluble salts	Yes, same CAS Yes, similar form No No
7440-36-0	Antimony	Yes	7440-36-0	Antimony & compounds, as Sb (handling & use)	Yes, same CAS
7440-38-2	Arsenic	Yes	7440-38-2	Arsenic compounds	Yes, same CAS
7440-39-3	Barium	No	7440-39-3	Barium, soluble compounds, as Ba	Yes, same CAS
7440-41-7	Beryllium	Yes	7440-41-7	Beryllium & compounds	Yes, same CAS

[7] A demonstration of compliance that applied IDAPA 58.01.01.210.20(a) and (b) to the sources of HAP emissions covered and addressed by the NESHAP is presented in the SOB (February 18, 2021).

Metal			TAP		
CAS	**Name**	**HAP?**	**CAS**	**Name**	**Is the Metal a TAP?**
7440-69-9	Bismuth	No	1304-82-1	Bismuth telluride undoped Bismuth telluride if selenium doped	No, Bi compounds are expected to be bismuthinite ($Bi2S_3$) and bismite (Bi_2O_3) [1]
7440-43-9	Cadmium	Yes	7440-43-9	Cadmium and compounds	Yes, same CAS
7440-70-2	Calcium	No	1317-65-3 156-62-7 1305-62-0 1305-78-8 1344-95-2 13397-24-5	Calcium carbonate Calcium cyanamide Calcium hydroxide Calcium oxide Calcium silicate (synthetic) Calcium sulfate	Yes [2] No, different CAS No, different CAS Yes [2] No, different CAS No, different CAS
7440-47-3	Chromium	Yes	7440-47-3 7440-47-3 16065-83-1 18540-29-9	Chromium metal, including: Chromium (II) compounds, as Cr Chromium (III) compounds, as Cr Chromium (VI) & compounds, as Cr+6	Yes, same CAS Yes, same CAS No, different CAS No, different CAS
7440-48-4	Cobalt	Yes	10210-68-1 16842-03-8 7440-48-4	Cobalt carbonyl, as Co Cobalt hydro carbonyl, as Co Cobalt metal, dust, and fume	No, different CAS No, different CAS Yes, same CAS
7440-50-8	Copper	No	7440-50-8	Copper: Fume Dusts & mists, as Cu	Yes, same CAS No Yes, similar form
7440-55-3	Gallium	No		Not listed	No
7439-89-6	Iron	No	1309-37-1 13463-40-6 7439-89-6	Iron oxide fume (Fe2O3), as Fe Iron pentacarbonyl, as Fe Iron salts, soluble, as Fe	No, different CAS No, different CAS Yes, same CAS
7439-91-0	Lanthanum	No		Not listed	No
7440-09-7	Potassium	No	1310-58-3	Potassium hydroxide	No, different CAS
7439-92-1	Lead	Yes		Not listed	No, criteria pollutant
7439-95-4	Magnesium	No	1309-48-4	Magnesium oxide fume	No, different CAS
7439-96-5	Manganese	Yes	7439-96-5	Manganese, as Mn, including: Dust & compounds Fume	Yes, same CAS Yes, similar form No
7439-97-6	Mercury	Yes		Not listed	No, regulated by mercury rules
7439-98-7	Molybdenum	No	7439-98-7	Molybdenum, as Mo, including: Soluble compounds Insoluble compounds	Yes, same CAS No Yes, similar form
7440-02-0	Nickel	Yes	7440-02-0 12035-72-2 7440-02-0	Nickel Nickel Subsulfide Nickel Refinery Dust	No, see Ni refinery dust No, different CAS Yes, same CAS and form

Metal			TAP		
CAS	**Name**	**HAP?**	**CAS**	**Name**	**Is the Metal a TAP?**
7723-14-0	Phosphorus	Yes	7723-14-0	Phosphorus	Yes, same CAS
			10025-87-3	Phosphorus oxychloride	No, different CAS
			10026-13-8	Phosphorus penta-chloride	No, different CAS
			1313-80-3	Phosphorus penta-sulfide	No, different CAS
			1314-56-3	Phosphorus pentoxide (ID)	No, different CAS
			7719-12-2	Phosphorus trichloride	No, different CAS
7782-49-2	Selenium	Yes	7782-49-2	Selenium and compounds, as Se	Yes, same CAS
7440-23-5	Sodium	No	26628-22-8	Sodium azide (CL)	No, different CAS
			7631-90-5	Sodium bisulfite	No, different CAS
			136-78-7	Sodium 2,4-dichloro-phenoxyethyl sulfate; see Sesone	No, different CAS
			62-74-8	Sodium fluoroacetate	No, different CAS
			1310-73-2	Sodium hydroxide	No, different CAS
			7681-57-4	Sodium metabisulfite	No, different CAS
7440-20-2	Scandium	No		Not listed	No
7440-24-6	Strontium	No		Not listed	No
7440-28-0	Thallium	No	7440-28-0	Thallium, soluble compounds, as Tl	Yes, same CAS
7440-29-1	Thorium	No		Not listed	No
7440-32-6	Titanium	No		Not listed	No
7440-33-7	Tungsten	No	7440-33-7	Tungsten, including: Insoluble compounds Soluble compounds	Yes, same CAS Yes, similar form No
7440-61-1	Uranium	No	7440-61-1	Uranium (natural) soluble & insoluble compounds, as U	Yes, same CAS
7440-62-2	Vanadium	No	1314-62-1	Vanadium, as V_2O_5 Respirable dust & fume	No, different CAS [3]
			12604-58-9	Ferrovanadium dust	No, different CAS
7440-66-6	Zinc	No	7440-66-6	Zinc metal (ID)	Yes, same CAS
			7646-85-7	Zinc chloride fume	No, different CAS
			1314-13-2	Zinc oxide fume	No, different CAS
			1314-13-2	Zinc oxide dust	No, different CAS

[1] Over 95% of the samples were at or below the detection limit for Bismuth of 2 ppm. Limited sampling for tellurium indicates 90% of the samples are below 0.5 ppm. Mineralogical studies have not identified telluride minerals as a significant phase in the deposits. Based on these low levels and deposit mineralogy, no significant bismuth telluride is expected to be found in the ore body or development rock.

[2] Although the CAS numbers do not match, the calcium in the ore, limestone, and aggregate is expected to be in the form of calcium carbonate ($CaCO_3$). For lime, the calcium will be in the form of calcium oxide (CaO).

[3] The principal vanadium mineral in Idaho shale-hosted vanadium deposits is metahewettite ($CaV_6O_{162} \bullet H2O$) (USGS n.d.). Although not a TAP, vanadium in the ore, limestone, and aggregate is conservatively assumed to be V_2O_5 for the purpose of the TAP evaluation included in this HAP/TAP Addendum.

3.3 Screening Level Analysis of TAP Emissions

As discussed in Section 2.0, the highest TAP emissions scenario is Model Scenario W3, that estimates emissions from a potential throughput of 180,000 T/day. Table A in Appendix A

provides a summary of the TAP emissions for Model Scenario W3, identifies whether the sources are covered or addressed by IDAPA 58.01.01.210.20(a) or (b) (Section 3.1), and notes the TAP screening EL. TAPs that exceed the screening EL are highlighted in Table A. These TAPs require further demonstrations of compliance with the applicable ambient air concentration (AAC) and are listed in Table 3 below.

Table 3. TAPs Exceeding the Screening Emission Level

CAS	TAP Name	Carcinogenic	SGP PTE (lb/hr) [1]	Screening EL (lb/hr)
7429-90-5	Aluminum	No	58.50	0.667
7440-38-2	Arsenic	Yes	0.544	0.0000015
7440-39-3	Barium	No	0.659	0.033
7440-41-7	Beryllium	Yes	0.00261	0.000028
7440-43-9	Cadmium	Yes	0.000435	0.0000037
1317-65-3	Calcium Carbonate	No	13.65	0.667
1305-78-8	Calcium Oxide	No	0.696	0.133
592-01-8	Cyanide	No	0.453	0.333
50-00-0	Formaldehyde	Yes	0.00189	0.00051
7439-89-6	Iron	No	15.04	0.067
7439-96-5	Manganese	No	0.244	0.067
7440-02-0	Nickel	Yes	0.00169	0.000027
7723-14-0	Phosphorus	No	0.530	0.007
7664-93-9	Sulfuric Acid	No	2.03	0.067
7440-28-0	Thallium	No	0.00867	0.007
7440-62-2	Vanadium	No	0.0237	0.003

[1] Model Scenario W3, 180,000 T/day Emissions

3.4 Modeling of TAP Emissions

To maintain consistency with the National Ambient Air Quality Standards (NAAQS) compliance analyses reviewed by IDEQ, the TAP modeling was performed using the same IDEQ-approved datasets and model versions described in the SOB from February 18, 2021. TAP modeling was conducted for the 14 modeling scenarios consistent with the NAAQS analyses. Scenario W5 was eliminated from the arsenic modeling, as discussed in Section 3.4.5.

3.4.1 Meteorological Data and Deposition

The meteorological dataset used for the TAP modeling was processed using EPA's Qian and Venkatram (Q&V) meteorological processing method. This method, which does not use the BULKRN keyword, is approved by EPA as a default method.

As discussed in the PTC application, EPA evaluated the performance of the model with the Q&V processed meteorological dataset as part of its model approval determination. This evaluation quantified the bias between the modeled concentrations and the actual observed concentrations. The results of EPA's evaluation showed a conservative bias of the model to overpredict concentrations by a factor of 1.41 to 3.21 (Air Sciences 2020, A-8 of Attachment A). Therefore, the meteorological dataset used in the TAP modeling is expected to predict conservatively high concentrations.

The particulate deposition parameters used in the NAAQS compliance analysis were derived for PM_{10} and $PM_{2.5}$. See Tables 24 and 25 in the SOB from February 18, 2021. Dust-related metal TAP emissions include total particulates (all size fractions of PM up to PM_{30}). Therefore, the deposition parameters for PM were calculated using the same methodology and EPA references used for PM_{10} and $PM_{2.5}$ in the NAAQS compliance analysis. The PM deposition parameters are provided in Table 4.

Table 4. PM Deposition Parameters by Source Category

Source Category	Parameter	PM				
		Bin 1	**Bin 2**	**Bin 3**	**Bin 4**	**Bin5**
Haul Roads	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.02	0.23	0.75	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (DR average of YP, HF, WE)	2.46	2.46	2.46	--	--
Material Handling (Ore, DR, Limestone)	Bin Upper Diameter (µm)	2.50	5.00	10.00	30.00	--
	Mass Fraction	0.07	0.20	0.20	0.53	--
	Mass Mean Diameter (µm)	2.50	5.00	10.00	30.00	--
	Density (g/cm^3) (Ore)	Pit-specific, see Table 5				
	Density (g/cm^3) (DR)	Pit-specific, see Table 5				
	Density (g/cm^3) (Limestone)	1.09	1.09	1.09	1.09	--
Baghouses	Bin Upper Diameter (µm)	2.50	6.00	10.00	30.00	--
	Mass Fraction	0.25	0.45	0.20	0.10	--
	Mass Mean Diameter (µm)	2.50	6.00	10.00	30.00	--
	Density (g/cm^3) (Ore)	Pit-specific, see Table 5				
Diesel Engines	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.82	0.08	0.03	0.03	0.04
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm^3) (Diesel Combustion)	1.00	1.00	1.00	1.00	1.00
Heaters and Boilers	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.23	0.22	0.25	0.09	0.21
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm^3) (Propane Combustion)	1.24	1.24	1.24	1.24	1.24
	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--

Source Category	Parameter	PM				
		Bin 1	Bin 2	Bin 3	Bin 4	Bin5
Lime Loading and Unloading (Quick, Pebble)	Mass Fraction	0.05	0.29	0.66	--	--
	Mass Mean Diameter	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Quick)	0.44	0.44	0.44	--	--
	Density (g/cm^3) (Pebble)	0.96	0.96	0.96	--	--
Lime Unloading (Quick, Pebble)	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.09	0.49	0.42	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Quick)	0.44	0.44	0.44	--	--
	Density (g/cm^3) (Pebble)	0.96	0.96	0.96	--	--
Cement and Aggregate Loading and Unloading	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.29	0.66	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Cement)	1.44	1.44	1.44	--	--
	Density (g/cm^3) (Aggregate)	1.28	1.28	1.28	--	--
Prill Loading and Unloading	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.30	0.65	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Prill)	0.84	0.84	0.84	--	--
Refining Processes	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.72	0.10	0.07	0.03	0.08
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm^3) (Diesel Combustion)	1.00	1.00	1.00	1.00	1.00
Portable Crushing and Screening Plant	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.32	0.63	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (DR average of YP, HF, WE)	2.46	2.46	2.46	--	--
Lime Kiln and Ball Mill	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction (Kiln)	0.27	0.28	0.45	--	--
	Mass Fraction (Ball Mill)	0.30	0.54	0.16	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3)	1.09	1.09	1.09	--	--
Blasting and Drilling	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.03	0.49	0.48	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Ore or DR)	Pit-specific, see Table 5				
Dozing	Bin Upper Diameter (µm)	2.50	10.00	15.00	30.00	--
	Mass Fraction	0.11	0.08	0.06	0.75	--
	Mass Mean Diameter (µm)	2.50	10.00	15.00	30.00	--
	Density (g/cm^3) (Waste)	Pit-specific, see Table 5				

Table 5. Pit-Specific Ore and DR Densities for Deposition

Pit	Material	Density (g/cm^3)
YP	Ore	2.59
BT	Ore	2.00
HF	Ore	2.59
WE	Ore	2.68
YP	DR	2.48
BT	DR	2.00
HF	DR	2.34
WE	DR	2.57
Average (YP, HF, WE)	DR	2.46

3.4.2 Modeling for Non-Carcinogenic TAPs

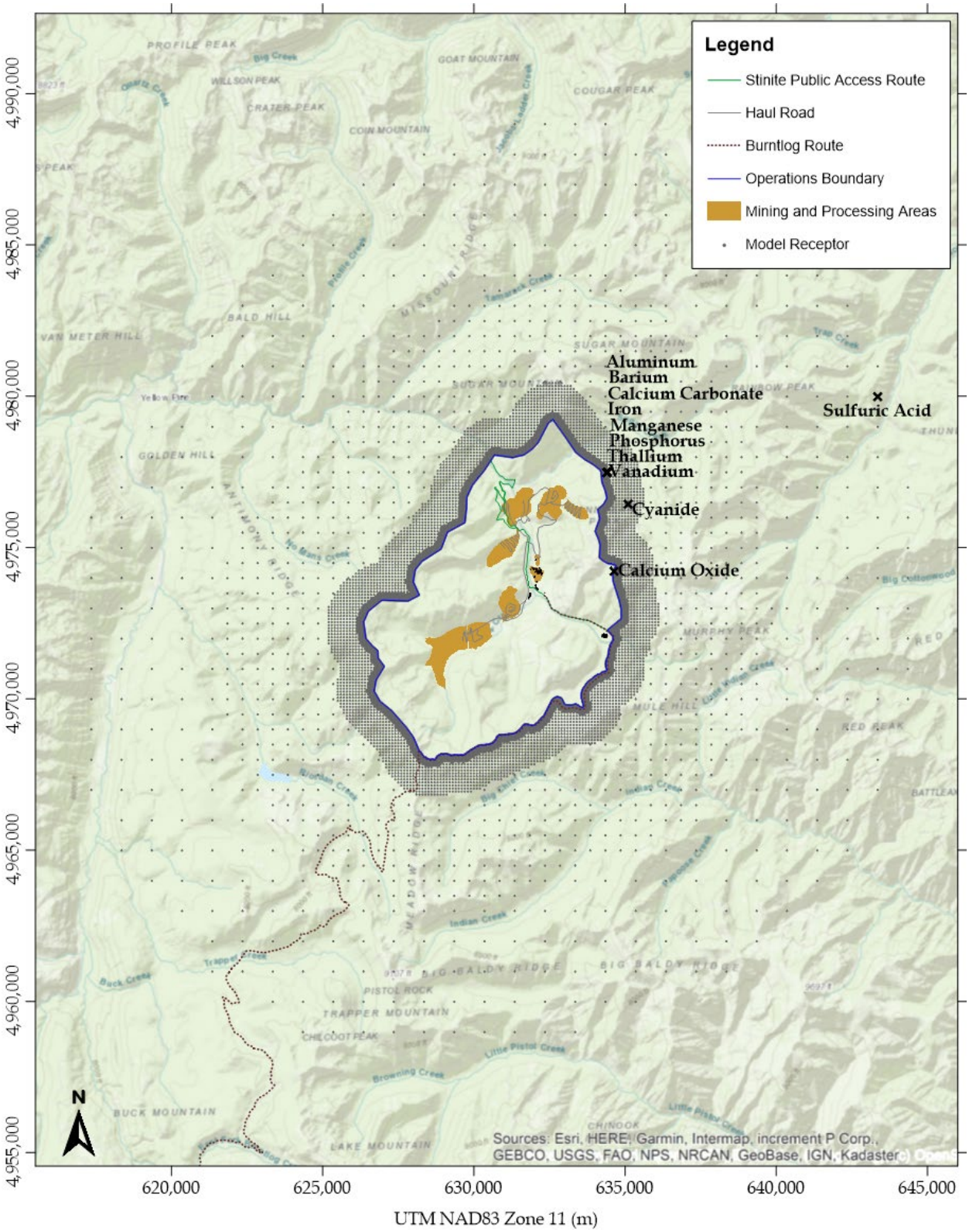
The non-carcinogenic TAPs subject to the AACs per IDAPA 58.01.01.585 were modeled at the emission levels shown in Table 3 above. The maximum 24-hour modeled concentration for each of the 14 modeling scenarios demonstrates compliance with the applicable AAC, as summarized in Table 6.

Table 6. Compliance Demonstration for Non-Carcinogenic TAPs

CAS	TAP Name	Highest Model Scenario	SGP Maximum 24-hr Concentration (μg/m³)	AAC (μg/m³)	TAP Compliance
7429-90-5	Aluminum	W5	6.17	500	Yes
7440-39-3	Barium	W5	0.07	25	Yes
1317-65-3	Calcium Carbonate	W5	1.22	500	Yes
1305-78-8	Calcium Oxide	ALL	0.15	100	Yes
592-01-8	Cyanide	ALL	0.20	250	Yes
7439-89-6	Iron	W5	1.58	50	Yes
7439-96-5	Manganese	W5	0.03	250	Yes
7723-14-0	Phosphorus	W5	0.06	5	Yes
7664-93-9	Sulfuric Acid	ALL	0.41	50	Yes
7440-28-0	Thallium	W5	0.001	5	Yes
7440-62-2	Vanadium	W5	0.002	2.5	Yes

The modeled emissions for each modeling scenario and source are provided in Appendix B. The modeled concentration per modeling scenario is provided in Appendix C. The predicted locations of the maximum concentrations for each non-carcinogenic TAP are presented in Figure 1.

Figure 1. Non-Carcinogenic Maximum TAP Concentration (µg/m³) Locations



3.4.3 Modeling Carcinogenic TAPs

The carcinogenic TAPs subject to the acceptable ambient concentrations for carcinogens (AACC) per IDAPA 58.01.01.586 were modeled using an emission inventory that includes the following T-RACT controls, long-term mining production limits, and other emission inventory refinements, as described below:

- Installing and operating dust collection systems on drilling rigs (T-RACT)
- Capping the haul roads that are outside of the pits and development rock storage facilities (DRSFs) with clean development rock (T-RACT)
- Limiting long-term mining production to 135,000 T/day (5-year rolling total)
- Constructing the Burntlog access road with offsite materials containing background level arsenic concentrations
- Updating the bulldozing emission factor using the SGP site-specific silt content.

The above emission inventory reductions are discussed in more detail in Section 5.0. The T-RACT analysis is provided in Section 6.0. A comparison of the 180,000 T/day TAP emissions shown in Table 3 and the T-RACT TAP emissions is shown in Table 7.

Table 7. Comparison of 180,000 T/day and T-RACT Emissions

CAS	TAP Name	Carcinogenic	180,000 T/day Emissions (lb/hr) [1]	T-RACT Emissions (lb/hr) [2]
7440-38-2	Arsenic	Yes	0.544	0.232
7440-41-7	Beryllium	Yes	0.00261	0.00185
7440-43-9	Cadmium	Yes	0.000435	0.000317
50-00-0	Formaldehyde	Yes	0.00189	0.00189
7440-02-0	Nickel	Yes	0.00169	0.00121

[1] Model Scenario W3 emissions from Table 3
[2] T-RACT emission levels for the demonstration of carcinogenic TAP compliance. See Table A-W3, T-RACT Emissions in Appendix A, pp. A-45 to A-49.

The maximum modeled concentration for each of the 14 modeling scenarios demonstrated compliance with the applicable AACC, as summarized in Table 8. The AACCs listed in Table 8 were increased by a factor of ten (10) per IDAPA 58.01.01.210.12(b); T-RACT adjustment. The SGP maximum concentrations were adjusted to account for the life-of-mine (LOM) production limits, which affect the lifetime exposure, and to account for the elimination of Modeling Scenario W5. See Sections 3.4.4 and 3.4.5 for more detail.

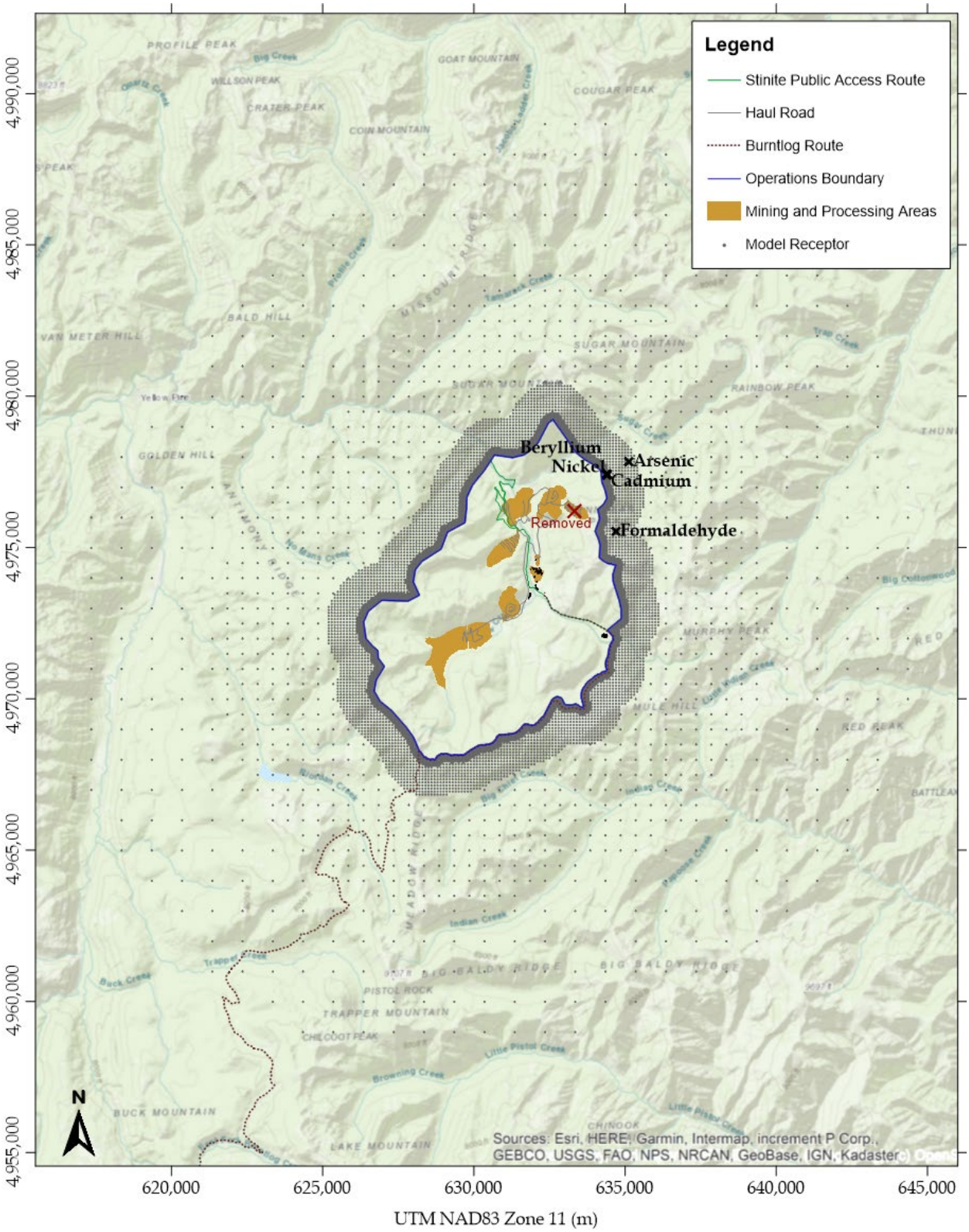
Table 8. Compliance Demonstration for Carcinogenic TAPs

CAS	TAP Name	Model Scenario	SGP Maximum Lifetime Exposure Concentration (μg/m³) [1]	AACC (μg/m³) [2]	TAP Compliance
7440-38-2	Arsenic	W2	0.00095	0.0023	Yes
7440-41-7	Beryllium	W1	0.00001	0.042	Yes
7440-43-9	Cadmium	W1	0.000002	0.0056	Yes
50-00-0	Formaldehyde	ALL	0.00007	0.77	Yes
7440-02-0	Nickel	W1	0.00001	0.42	Yes

[1] The lifetime exposure concentrations are based on the proposed restrictions discussed in Sections 3.4.4 and 3.4.5.
[2] The AACCs are increased by a factor of ten per IDAPA 58.01.01.210.12(b); T-RACT adjustment.

The modeled emissions for each modeling scenario and source are provided in Appendix B. The modeled concentration per modeling scenario is provided in Appendix C. The locations of the maximum concentrations for each carcinogenic TAP are presented in Figure 2.

Figure 2. Carcinogenic Maximum TAP Concentration (µg/m³) Locations



3.4.4 Carcinogenic TAP Modeling Lifetime Exposure Adjustment

The AACCs provided in IDAPA 58.01.01.586 were developed *based on the probability of developing excess cancers over a seventy (70) year lifetime exposure to one (1) microgram per cubic meter (1 ug/m3) of a given carcinogen and expressed in terms of a screening emission level or an acceptable ambient concentration for a carcinogenic toxic air pollutant* (IDAPA 58.01.01.006.125). Therefore, the highest modeled annual carcinogenic TAP concentration from each of the 14 modeling scenarios was evaluated for lifetime exposure as follows:

$$Lifetime\ expsoure\ \left(\frac{\mu g}{m^3}\right) = \frac{Highest\ annual\ concentration\ \left(\frac{\mu g}{m^3}\right) \times 16\ (mine\ operation\ years)}{70\ (years, lifetime\ exposure)}$$

This equation conservatively assumes that the highest annual concentration from the 14 modeling scenarios is repeated for 16 years of mining operation. This is then averaged over 70 years to calculate the 70-year lifetime exposure.

Calculating lifetime exposure based on 16 years of mining operation is also conservative. The annual emissions for carcinogenic TAP modeling are based on 135,000 T/day (see Section 3.4.3) and 365 days per year. Over 16 years, this equates to a potential mining production of 788.4 million tons:

$$\frac{135{,}000\left(\frac{ton}{day}\right) \times 365\left(\frac{day}{year}\right) \times 16\ years}{1{,}000{,}000\left(\frac{ton}{million\ ton}\right)} = 788.4\ million\ tons$$

The actual LOM total production as described in the SGP Refined Proposed Action (ModPRO2) mine plan is only 402.86 million tons (Perpetua 2021a), which is 51.1% of the potential LOM production represented in the above equation and related emissions evaluations.

3.4.5 Arsenic Compliance Demonstration for Modeling Scenarios W1–W5

To demonstrate compliance with the AACC for arsenic, two addition operating limitations were applied:

- The removal of Modeling Scenario W5 as a potential operating scenario
- Limiting the West End pit's LOM potential mining production to 50% of the total LOM potential mining production of 788.4 million tons: 50% * 788.4 = 394.2 million tons

Perpetua Resources has determined that the West End DRSF will not be constructed. This change eliminated Modeling Scenario W5 from the arsenic modeling evaluation. The remaining four West End pit modeling scenarios (W1–W4) are evaluated using the 70-year lifetime exposure equation from Section 3.4.4 and adjusting for the proposed West End pit LOM production limit of 50% of the total production as follows:

$$lifetime\ expsoure\ \left(\frac{\mu g}{m^3}\right) = \left(\frac{\left[Wi\left(\frac{\mu g}{m^3}\right)(50\%) + nonW\left(\frac{\mu g}{m^3}\right)(50\%)\right] \times 16\ (mine\ operation\ years)}{70\ (years, lifetime\ exposure)}\right)$$

Where:

$Wi = the\ modeled\ annual\ arsenic\ concentration\ from\ Scenario\ Wi;\ i = 1\ to\ 4$

$nonW = the\ modeled\ annual\ arsenic\ concentration\ of\ the\ highest\ nonW\ scenario;$

B1, B2, H1, H2, H3, H4, Y1, Y2, or Y3

The above equation was used to calculate the lifetime arsenic exposure from the West End pit scenarios (W1–W4) on a receptor-by-receptor basis. Combining the concentrations from Modeling Scenarios W1–W4 with the highest concentration from the remaining non-West End pit scenarios (B1, B2, H1, H2, H3, H4, Y1, Y2, or Y3) ensures that the maximum concentration is evaluated.

Calculating lifetime arsenic exposure based on the proposed West End pit LOM production limit of 50% of the total production is conservative. The actual LOM total production from the West End pit as described in the ModPRO2 mine plan is only 198.26 million tons (Perpetua 2021a), which is 50.3% of the proposed West End pit LOM production limit of 394.2 million tons.

4.0 COMPARISON OF ACTUAL ARSENIC MODELING TO POTENTIAL ARSENIC MODELING

Additional analyses of arsenic emissions were prompted by public comments on the draft PTC. IDEQ requested that Perpetua Resources conduct an arsenic modeling analysis based on the actual mining operation and production described in the ModPRO2 mine plan. Those modeling results were submitted to IDEQ in a report on July 8, 2021, titled "Stibnite Gold Project Permit to Construct Application Arsenic Modeling Addendum" (Air Sciences 2021).

While that report provided an assessment of the actual arsenic concentrations expected from the actual mining operation and production over the life of the SGP ("actual analysis"), the analysis described in Section 3.0 above is based on potential operating scenarios ("potential analysis"). These analyses ensure that public health is protected under all operating conditions.

A comparison between the actual analysis and the potential analysis for the lifetime exposure of arsenic is summarized in Table 9.

Table 9. Actual Analysis vs. Potential Analysis for Arsenic Lifetime Exposure

Model Parameter	Actual Data	Potential Data	Actual Data Basis	Potential Data Basis
Process emissions (lb/hr)	0.004514	0.004514	Equipment design rate	Equipment design rate
Mining emissions (lb/hr); varies	Max: 0.0854 Min: 0.0058 Avg: 0.0451	Max: 0.232 Min: 0.061	ModPRO2 – 16 years of operation	14 potential worst-case scenarios
Emissions included in modeling (lb/yr)	100%	98%	Actual analysis of all emissions	Includes IDAPA 58.01.01.210.20
LOM production (million tons)	402.86	788.4	ModPRO2	135,000 ton/day * 365 day/yr * 16 years
Lifetime exposure modeling	Average concentration over 16 years of operation	Highest scenario concentration assumed for 16 years	Actual analysis	Potential worst-case analysis
Maximum modeled concentration ($\mu g/m^3$)	0.00015	0.00095	Actual analysis	Potential worst-case analysis
Applicable AACC ($\mu g/m^3$)	0.0023	0.0023	IDAPA 58.01.01. 210.12(b) and .586	IDAPA 58.01.01. 210.12(b) and .586

A brief discussion of Table 9 is provided below:

- AACC Results: In both the actual and potential analyses, the maximum modeled arsenic concentrations are below the AACC, demonstrating compliance with IDAPA 58.01.01.210.

- Process emissions: The process arsenic emissions in both analyses are identical. This is because both emission inventories were based on the maximum design rates of the process equipment.

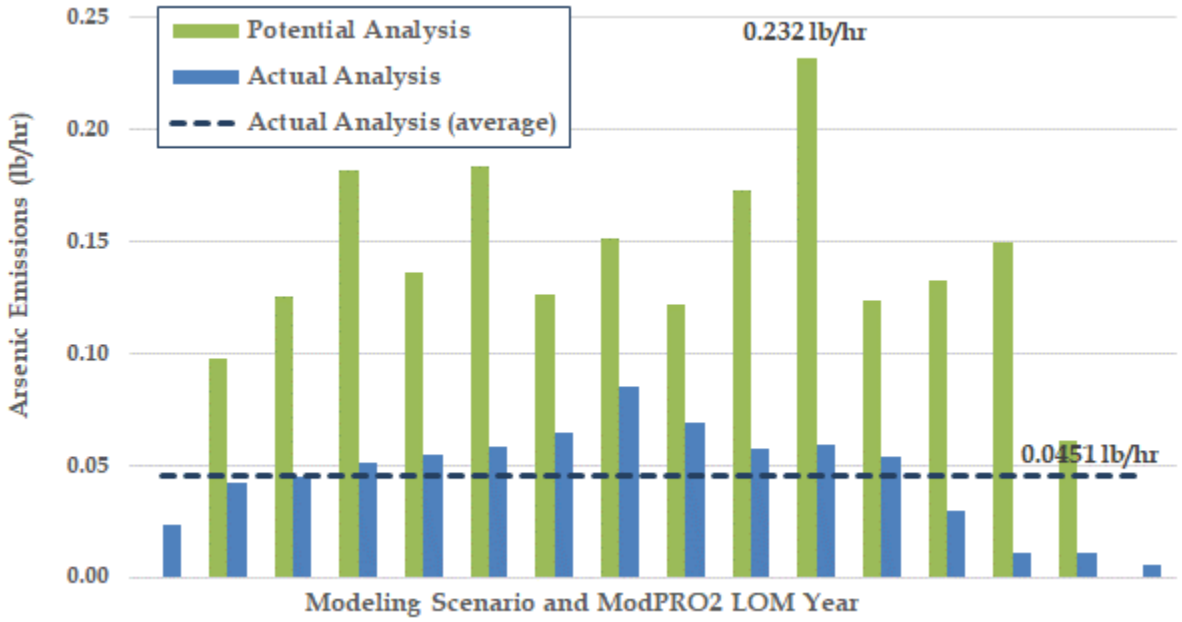
- Mining emissions: The arsenic emissions in the actual analysis (0.0451 lb/hr average) are only 19% of the arsenic emissions in the potential analysis (0.232 lb/hr highest scenario). This is because the actual mining operation and production activities (e.g., drilling, blasting, material product, hauling miles, etc.) in ModPRO2 are far less than the potential mining (PTC) operating scenarios. Figure 3 compares the ModPRO2 arsenic emissions from mining for each year of operation (actual analysis) to the PTC arsenic emissions from mining for each worst-case operating scenario (potential analysis).

- In both analyses, all the arsenic emissions are included in the modeling, except emissions from covered or addressed sources, IDAPA 58.01.01210.20(a) and (b). See Section 3.1.

- The actual analysis LOM production of 402.86 million tons is 51.1% of the potential analysis production of 788.4 million tons.

- When modeling the lifetime arsenic exposure, the actual analysis is based on modeling each year of the ModPRO2 mine plan and then averaging the yearly results on a receptor-by-receptor basis. In addition to the lower actual arsenic emissions, the mining activity locations vary, which reduced the average arsenic concentration at any given location outside the operations boundary. In contrast, the potential analysis is based on higher (potential) emissions and the highest modeling scenario, which are assumed to occur for 16 consecutive years. This potential approach resulted in significantly higher and more conservative arsenic hot-spot concentrations.

Figure 3. Actual Arsenic Mining Emissions vs. Potential Arsenic Mining Emissions



The concentrations and maximum locations of the arsenic lifetime exposure (70 years) are presented in Figure 4 for the actual analysis and Figure 5 for the potential analysis. As shown in these figures, the maximum arsenic concentrations are below the applicable AACC per IDAPA 58.01.01.210.12(b) and 586.

Figure 4. Actual Arsenic Concentrations (µg/m³) and Maximum Location

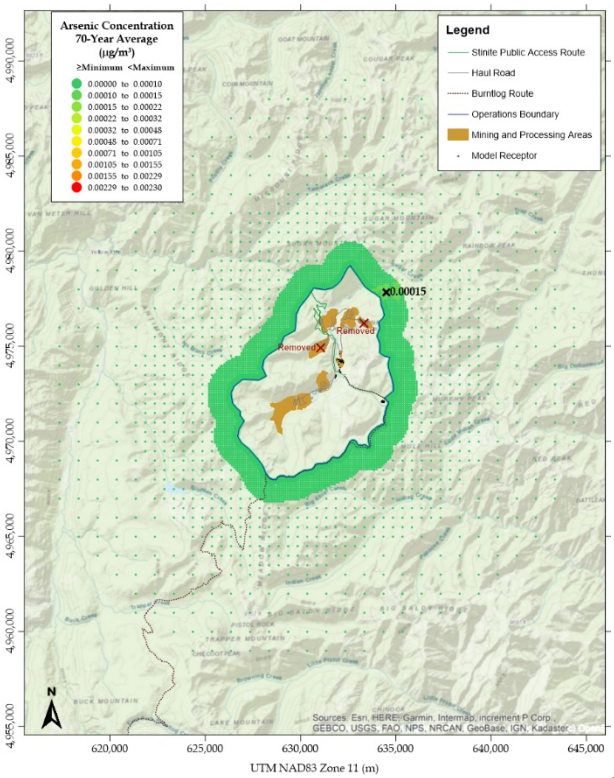
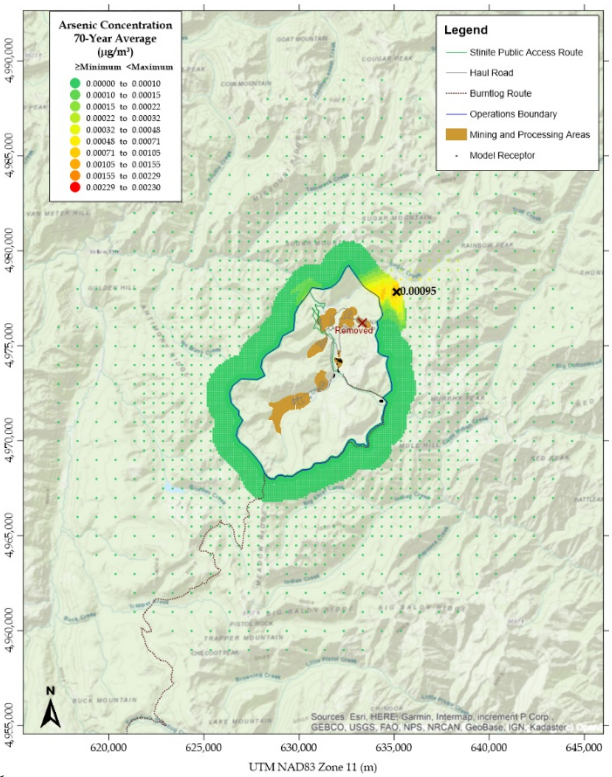


Figure 5. Potential Arsenic Concentrations (µg/m³) and Maximum Location



5.0 EMISSION INVENTORY FOR CARCINOGENIC TAPS

As discussed in Section 3.4.3, carcinogenic TAPs were modeled using an emission inventory adjusted for T-RACT controls, long-term mining production limits, and other refinements. These emission inventory changes are described in the following sections. The detailed emission calculations for the T-RACT emission inventory are provided in Appendix A (HAP/TAP Emission Calculations – Scenario W3, T-RACT Emissions).[8] The changes to these emission inventory inputs are highlighted on page A-41 of Appendix A.

5.1 Drilling Dust Control System

To reduce dust-related metal TAP emissions from drilling, Perpetua Resources will install and operate drilling rigs mounted with dust collection systems. *These systems have the ability to operate in various climates, i.e., they are not subject to freezing at lower temperatures as with the use of water, and they can be up to 99 percent efficient if properly maintained* (CDC 2012). The arsenic emissions inventory in Appendix A conservatively assumes a dust control efficiency of 90% for these systems.

5.2 Haul Road Capping

To reduce dust-related arsenic emissions from haul roads, Perpetua Resources will cap the haul roads that are outside of the pits and DRSFs with clean (low arsenic) development rock. Haul roads within the pits and DRSFs cannot be capped with this material because of steep grades and periodic road rerouting as mining areas develop. The median arsenic concentration of the clean development rock is 90 parts per million (ppm) (Perpetua 2021g).

5.3 Long-Term Mining Production Limits

To limit long-term dust-related metal TAP emissions, Perpetua Resources proposes limiting mining production to 135,000 T/day based on a 5-year rolling averaging period. This long-term mining production limit will be in addition to the current short-term daily limit of 180,000 T/day.

Limiting the long-term mining production limit to 135,000 T/day (5-year rolling average) is conservative. The highest 5-year rolling average mining production rate as described in ModPRO2 is only 95,700 T/day (Perpetua 2021a), which is 70.9% of the proposed limit.

[8] HAP/TAP Emission Calculations – Scenario W3, T-RACT: The HAP and TAP emissions based on T-RACT controls, a long-term mining production limit of 135,000 T/day (5-year rolling average), other refinements, and the highest emissions scenario (Modeling Scenario W3).

5.4 Burntlog Access Road Refinement

To reduce dust-related arsenic emissions from vehicle travel on the Burntlog access road, Perpetua Resources will construct this road with borrow material located outside of the mine site ambient air boundary. Analyses of the borrow sites show low arsenic levels of 2.5 ppm (ALS 2018), which are consistent with the background soil levels (DHHS 2007).

5.5 Bulldozing Refinement

Perpetua Resources and Air Sciences conducted a thorough review of the SGP emissions inventory to identify any potential dust-related metal TAP emission control measures (as discussed in the previous sections) and emission factor refinements. The only emission factor refinement identified was changing the bulldozing emission factor silt content from the EPA default of 6.9% to the SGP site-specific silt content of 4.0% (Midas Gold 2015). EPA recommends the use of site-specific data when available.[9]

[9] *In using the equations to estimate emissions from sources found in a specific western surface mine, it is necessary that reliable values for correction parameters be determined for the specific sources of interest if the assigned quality ratings of the equations are to be applicable. For example, actual silt content of coal or overburden measured at a facility should be used instead of estimated values. In the event that site-specific values for correction parameters cannot be obtained, the appropriate geometric mean values from Table 11.9-3 may be used, but the assigned quality rating of each emission factor equation should be reduced by 1 level (e.g., A to B)* (EPA 1998).

6.0 T-RACT ANALYSIS

Per IDAPA 58.01.01.210.14(a), this section documents the T-RACT control technologies.

6.1 Drilling Dust Control System

As discussed in Section 5.1, Perpetua Resources will install and operate drilling rigs mounted with dust collection systems. The following paragraphs evaluate this control as T-RACT:

Identification of all possible control technologies

Drilling operations create dust-related metal TAP emissions. The possible control technologies for these emissions are as follows:

- Applying best management practices
- Wet drilling with water injection
- Dry drilling with dust collectors

Best management practices include: (1) avoiding drilling operations during high dust conditions, and (2) shrouding drill areas to limit dust emissions.

Wet drilling includes injected water flows through the center of the drill and out though the drill bit to reduce dust emissions by 96% to 98%.[10]

Dry drilling includes rigs equipped with dust collection systems that shroud dust generated from the drilling area, capture, and remove dust through a dust collection system composed of an exhaust fan and filters that can achieve up to 99% control efficiency (CDC 2012).

Elimination of technologically infeasible or unreasonable technologies

Wet drilling at the SGP has the following disadvantages:

- It is subject to freezing at the low temperatures expected for the SGP location.
- It can result in drill bit plugging, drill rotation binding, and drill bit degradation.
- A wet drill hole can interfere with the blasting agent.

Based on the above disadvantages of wet drilling, it is considered an infeasible or unreasonable technology for the SGP.

[10] *Testing has demonstrated that dust control efficiencies of up to 98 percent can be obtained using the water separator sub while dust control efficiencies of wet drilling without the water separator sub were 96 percent* (CDC 2012).

Ranking the remaining technologies by control effectiveness

The ranking of the possible control technologies for drilling by control effectiveness is as follows (highest to lowest):

1. Dry drilling with dust collectors – up to 99% control efficiency
2. Best management practices

Evaluation of the most effective control technology and selection of T-RACT

Perpetua Resources selects the top (most effective) control technology of dry drilling with dust collectors as T-RACT. Selecting the top control negates the need for considering economic, energy, and environmental impacts regarding the other control technologies.

6.2 Haul Road Dust and Arsenic Control

Dust emissions from unpaved roads are caused by vehicle traffic on these roads. Particles are lifted and dropped from the rolling wheels, and the turbulent wake behind the vehicles causes these particulates to become air borne. Dust control options include surface improvement (paving) or surface treatment (chemical suppressant application or watering).

As discussed in the SOB from February 18, 2021, Perpetua Resources will control dust emissions from haul roads by treating the surface with frequent watering and the periodic application of a chemical suppressant. Reducing dust emissions reduces dust-related metal TAP emissions. In addition, Perpetua Resources will reduce arsenic emissions by capping the haul roads outside of the pits and DRSFs with clean (low arsenic) development rock, as discussed in Section 5.2. The following sections evaluate these control measures as T-RACT.

6.2.1 Dust Control Technologies

Identification of all possible control technologies

Vehicle traffic on unpaved haul roads creates dust-related metal TAP emissions. The possible control technologies for these emissions are as follows:

- Paving
- Application of a chemical dust suppressant
- Watering

Paving: *The control efficiencies achievable by paving can be estimated by comparing emission factors for unpaved and paved road conditions* (EPA 2006). The particulate emission factor for a paved road with a silt loading of 0.2 g/m^2 (based on the EPA default value for the SGP average daily traffic of 500–5,000 trips per day) (EPA 2011a) and the SGP average vehicle weight of 182.6 tons is

0.515 lb/VMT. The SGP unpaved road particulate emission factor is 14.43 lb/VMT (uncontrolled). Based on these emission factors, the estimated control efficiency of paving the haul roads is 96%.

Dust suppressant and watering: The SGP dust emissions from unpaved haul roads are calculated based on a surface treatment control efficiency of 90% (annual basis) for the application of a chemical dust suppressant supplemented with frequent watering. As discussed in the SGP Application, this control efficiency is supported by EPA's AP-42 13.2.2 referenced test reports, which show that a chemical dust suppressant alone can achieve 90% to 99% control efficiency and 98% for magnesium chloride in particular (Air Sciences 2020, Appendix A to Attachment A). A control efficiency of 90% is also supported by the control efficiency limits established under Reasonable Achievable Control Technology (RACT), Best Available Control Technology (BACT), and Lowest Achievable Emission Rate (LAER) determinations under EPA's New Source Review permitting program.

The EPA RACT/BACT/LAER Clearinghouse (RBLC) database contains case-specific information on the air pollution technologies required by major stationary sources seeking a permit under EPA's New Source Review (NSR) program. This database was queried for all listings of air pollution technologies for unpaved roads using chemical dust suppressants or a combination of chemical dust suppressants and watering. The results of the query identified 10 projects containing a control efficiency of 90% or greater for unpaved roads. These determinations are listed in Table 10.

Table 10. EPA RBLC Determinations for 90% or Greater Control Efficiency of Unpaved Roads

State	Facility Name	RBLC-ID	Dust Control	Dust Control Efficiency
AK	Donlin Gold Project	AK-0084	water/chem	90%
AR	Turk Power Plant	AR-0094	water/chem	90%
CO	Rio Grande Portland Cement Corp.	CO-0043	water/chem	90%
IN	Nucor Steel	IN-0034	chem	90%
LA	Nucor Steel Louisiana	LA-0239	water/chem	90%
MO	Lafarge Corp.	MO-0048	chem	90%
NV	Sloan Quarry	NV-0045	chem	98%
NV	Nellis Air Force Base	NV-0047	water/chem	90%
OH	Unlimited Concrete	OH-0126	water/chem	90%
OH	Unlimited Concrete	OH-0131	water/chem	90%

(EPA 2021)

Elimination of technologically infeasible or unreasonable technologies

Paving haul roads at the SGP has the following disadvantages:

- The paving of haul roads is not conventional practice at mining operations.
- Paved highway weight limits are only approximately 20,000 pounds (10 tons).
- Paving is costly.

The conventional practice for mining operations is to utilize unpaved haul roads with treated surfaces to control fugitive dust. Haul trucks are single axle vehicles with a gross loaded weight of 60 tons to 685 tons. The loaded weight range for the SGP haul trucks is 60 to 260 tons. These weights significantly exceed regulatory weight limits for paved highways of 10 tons. Furthermore, the SGP mining activity locations move as mining progresses. This requires haul roads to be rerouted as necessary. Due to the temporary nature of hauling routes and the heavy weight of haul trucks, paving is considered an infeasible or unreasonable technology for the SGP.

Ranking the remaining technologies by control effectiveness

The ranking of the possible control technologies for drilling by control effectiveness is as follows (highest to lowest):

1. Application of a chemical dust suppressant – 90% to 99% control efficiency

2. Watering – 75% to 95% control efficiency (EPA 2006, Figure 13.2.2-2)

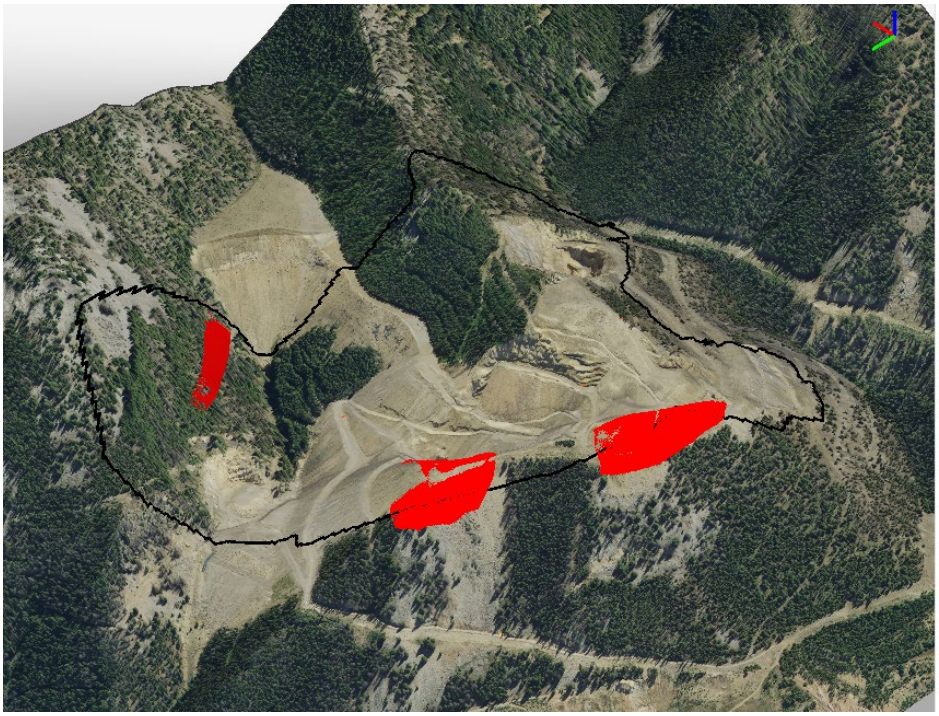
Evaluation of the most effective control technology and selection of T-RACT

After eliminating paving as a viable control option, Perpetua Resources selects the next most effective control technologies of the application of a chemical dust suppressant supplemented with frequent watering as T-RACT.

6.2.2 Arsenic Control Technologies

After applying T-RACT for dust control, as discussed in Section 6.2.1, dust-related arsenic emissions can only be further reduced by capping the haul roads with clean (low-arsenic) development rock. The median arsenic concentration of the SPG onsite material is 667 ppm (Midas Gold 2017c). However, there are quartzite rock deposits at the West End pit that have significantly lower mineralization and, thus, lower arsenic levels. The median arsenic concentration of this quartzite rock is 90 ppm (Perpetua 2021g), and there is approximately 3 million tons of this material available. Figure 6 shows the locations of the quartzite rock deposits.

Figure 6. Quartzite Rock Areas



Perpetua Resources proposes capping the haul roads that are outside of the pits and DRSFs with clean (low-arsenic) development rock as a T-RACT work practice, in addition to the T-RACT dust control measures discussed in Section 6.2.1. Haul roads within the pits and DRSFs cannot be capped with this material because of steep grades and periodic road rerouting as mining areas develop.

7.0 PROPOSED PERMIT CONDITIONS FOR CARCINOGENIC TAP COMPLIANCE

IDEQ is required to establish limits and standards as part of the permit to construct to ensure compliance with the TAP provisions in accordance with IDAPA 58.01.01.210.12(d) and 14(e). Per these two rules, Perpetua Resources proposes the following permit conditions:

7.1 Conditions per IDAPA 58.01.01.210.12(d)

Per IDAPA 58.01.01.210.12(d), *[t]he Department shall include emission limits and other permit terms for the toxic air pollutant in the permit to construct that assure that the facility will be operated in the manner described in the preconstruction compliance demonstration*. As discussed in Section 5.2, Perpetua Resources is proposing long-term mining production limits to demonstrate compliance with carcinogenic TAPs. The following are proposed permit conditions to address this TAP provision:

- The permittee shall haul no more than 135,000 tons per day (T/day) of ore and rock, based on a 5-year rolling average.
    - Each year, the permittee shall monitor and record the amount of ore and rock transported on haul trucks in tons per year (T/yr), and calculate the 5-year rolling average (T/day) based on 365 days per year.
- The permittee shall haul no more than 788.4 million tons (MT) of ore and rock from all deposits over the life of the mine.
- The permittee shall haul no more than 394.2 MT of ore and rock from the West End deposit over the life of the mine.
    - Each year, the permittee shall monitor and record the amount of ore and rock transported on haul trucks (T/yr) from all deposits and the amount of ore and rock transported on haul trucks (T/yr) from the West End deposit, and calculate the life-of-mine rolling total (MT) for each.

7.2 Conditions per IDAPA 58.01.01.210.14(e)

Per IDAPA 58.01.01.210.14(e), *[i]f the Department determines that the applicant has proposed T-RACT, the Department shall determine which of the options, or combination of options, will result in the lowest emission of toxic air pollutants, develop the emission standards constituting T-RACT and incorporate the emission standards into the permit to construct.* As discussed in Section 6.2, Perpetua Resources is proposing T-RACT controls to demonstrate compliance with carcinogenic TAPs. The following are proposed permit conditions to address this TAP provision:

- The permittee shall use drilling rigs equipped with dust collection systems. Control efficiency: 90%.
    - Within 60 days after startup, the permittee shall develop and maintain an Operation and Maintenance (O&M) manual. The O&M manual shall be a permittee-developed document based upon, but independent from, manufacturer-supplied operating manuals. The permittee shall operate the dust collection systems in accordance with the O&M manual at all times. The requirements in the O&M manual shall be incorporated by reference to this permit and shall be enforceable permit conditions. The O&M manual shall be submitted to DEQ within 60 days after initial startup.
- The permittee shall cap haul roads that are outside of the pits and DRSFs with low-arsenic material.
    - The permittee shall develop and maintain a plan that:
        - identifies the low-arsenic quartzite rock deposits in the West End pit based on core sample analyses,
        - requires periodic inspections (at least quarterly) of the capped haul roads and recapping as needed, and
        - includes record keeping of the inspections and any recapping of roads, noting the date and road section.
    - The permittee shall use the low-arsenic quartzite rock deposits from the West End pit, or other material with equal or lower arsenic concentration, as capping material.
        - If other material is used, it must be analyzed for arsenic concentration and a record of the median arsenic concentration shall be maintained.

The Draft PTC currently includes conditions for treating haul road surfaces with a chemical suppressant and water to control 90% of the dust (on an annual basis). See Conditions 1.2, 2.1–2.6, 2.8, 3.2, and 3.9. Therefore, no new conditions are needed or proposed for this dust control practice.

8.0 MERCURY EMISSIONS ANALYSIS

A complete inventory of mercury emissions is provided in Appendix A, as discussed in Section 2.0. This section categorizes these emissions into mercury emissions covered or not covered by IDAPA 58.01.01.215. According to IDAPA 58.01.01.215:

No owner or operator may commence construction or modification of a stationary source or facility that results in an increase in annual potential emissions of mercury of twenty-five (25) pounds or more unless the owner or operator has obtained a permit to construct under Sections 200 through 228 of these rules. The permit to construct application shall include an MBACT analysis for the new source or sources for review and approval by the Department. A determination of applicability under Section 215 shall be based upon the best available information. Fugitive emissions shall not be included in a determination of applicability under Section 215.

01. Exemptions. New or modified stationary sources within a source category subject to 40 CFR Part 63 are exempt from the requirements of Section 215.

Table 11 summarizes the SGP mercury sources and potential emissions for the highest emissions year (Model Scenario W3, 180,000 T/day Emissions). This table also provides the mercury emissions without considering the above exemptions, the exemption criteria, and the non-exempt mercury emissions for each source. As shown in this table, under IDAPA 58.01.01.215.01, the total potential non-exempt mercury emissions are 5.40E-5 ton/yr (0.108 lb/yr), which is well below the 25 lb/yr emission threshold.

Table 11. Mercury Source and Emissions Summary

Source	All Emissions ton/yr	Fugitive/ NESHAP Exemption	Non-Exempt Emissions ton/yr
Mining			
Fugitive Dust (drilling, blasting, excavating, hauling, etc.)	0.0021	Fugitive	0
Fugitive Evaporative (pits, tailings, DRSFs, stockpiles)	0.0036	Fugitive	0
Ore Processing			
Crushing, Screening, and Transfers	2.47E-05		2.47E-05
Prill Silos	0		0
Ore Concentration and Refining			
Autoclave	0.00010	7E	0
EW, Pregnant Tank, Retort, Furnace, Carbon Kiln	0.0017	7E	0
Process Heating			
POX, Carbon Kiln, Propane Vaporizers, Solution Heater	8.28E-06		8.28E-06
Lime Production			
Lime Kiln Combustion	2.09E-05	5A	0
Limestone Crushers, Screens, Mill, and Transfers	3.86E-07		3.86E-07
Lime Kiln, Kiln Feed, Lime Mill, and Pebble Lime Silo	0.0010	5A	0
Lime Silos and Lime Mill Crushing	4.05E-09		4.05E-09
Aggregate Production			
Portable Crushers, Screens, and Transfers	1.10E-07		1.10E-07
Concrete Production			
Central Mixer	0		0
Cement Silo Loading and Unloading	0		0
Aggregate Bin	6.90E-08		6.90E-08
HVAC			
Heaters	2.04E-05		2.04E-05
Emergency Power			
Emergency Generators and Fire Pump	0	4Z	0
Fuel Storage			
Gasoline Fuel Tanks	0	6C	0
Total	**0.00863**		**5.40E-05**

9.0 REFERENCES

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Appendix A – HAP/TAP Emission Calculations

Appendix A Table of Contents

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 1 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

Model Scenario W3 180,000 T/day Emissions

Hazardous Air Pollutants (HAP)/Toxic Air Pollutants (TAP) Emissions Summary

		Emissions[1]									
		Fuel Combustion		Process/Prod/Leach		Mining		Total			
CAS	**HAP/TAP**	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	HAP	TAP
106-99-0	1,3-Butadiene	8.4E-07	3.7E-06	0	0	0	0	8.4E-07	3.7E-06	Y	Y
91-57-6	2-Methylnaphthalene	1.1E-06	4.6E-06	0	0	0	0	1.1E-06	4.6E-06	Y	N
56-49-5	3-Methylchloranthrene	7.8E-08	3.4E-07	0	0	0	0	7.8E-08	3.4E-07	Y	Y
57-97-6	7,12-Dimethylbenz(a)anthracene	7.6E-07	3.0E-06	0	0	0	0	7.6E-07	3.0E-06	Y	N
83-32-9	Acenaphthene	5.7E-06	7.1E-06	0	0	0	0	5.7E-06	7.1E-06	Y	N
208-96-8	Acenaphthylene	1.1E-05	1.4E-05	0	0	0	0	1.1E-05	1.4E-05	Y	N
75-07-0	Acetaldehyde	2.5E-05	1.1E-04	0	0	0	0	2.5E-05	1.1E-04	Y	Y
107-02-8	Acrolein	1.6E-05	2.0E-05	0	0	0	0	1.6E-05	2.0E-05	Y	Y
120-12-7	Anthracene	1.7E-06	2.4E-06	0	0	0	0	1.7E-06	2.4E-06	Y	N
7440-36-0	Antimony	0	0	5.7E-04	2.5E-03	1.9E-02	8.2E-02	1.9E-02	8.5E-02	Y	Y
7440-38-2	Arsenic	8.7E-06	3.8E-05	4.5E-03	2.0E-02	0.54	2.38	0.55	2.40	Y	Y
56-55-3	Benz(a)anthracene	3.1E-07	1.4E-06	0	0	0	0	3.1E-07	1.4E-06	Y	Y
71-43-2	Benzene	3.6E-04	1.6E-03	7.0E-03	3.1E-02	0	0	7.4E-03	3.2E-02	Y	Y
50-32-8	Benzo(a)pyrene	1.4E-07	6.1E-07	0	0	0	0	1.4E-07	6.1E-07	Y	Y
205-99-2	Benzo(b)fluoranthene	4.4E-07	1.9E-06	0	0	0	0	4.4E-07	1.9E-06	Y	Y
191-24-2	Benzo(g,h,i)perylene	7.5E-07	1.1E-06	0	0	0	0	7.5E-07	1.1E-06	Y	N
207-08-9	Benzo(k)fluoranthene	1.5E-07	6.6E-07	0	0	0	0	1.5E-07	6.6E-07	Y	Y
7440-41-7	Beryllium	5.2E-07	2.3E-06	4.3E-04	1.9E-03	2.6E-03	1.1E-02	3.0E-03	1.3E-02	Y	Y
92-52-4	Biphenyl	0	0	4.4E-05	1.9E-04	0	0	4.4E-05	1.9E-04	Y	Y
7440-43-9	Cadmium	4.8E-05	2.1E-04	4.1E-04	1.8E-03	4.1E-04	1.8E-03	8.7E-04	3.8E-03	Y	Y
75-15-0	Carbon Disulfide	0	0	1.4E-02	6.3E-02	0	0	1.4E-02	6.3E-02	Y	Y
7440-47-3	Chromium	6.6E-05	2.7E-04	6.1E-04	2.5E-03	7.3E-03	3.2E-02	8.0E-03	3.5E-02	Y	Y
18540-29-9	Cr (VI)	0	0	3.4E-07	1.5E-06	0	0	3.4E-07	1.5E-06	Y	Y
218-01-9	Chrysene	5.8E-07	2.5E-06	0	0	0	0	5.8E-07	2.5E-06	Y	Y
7440-48-4	Cobalt	4.0E-06	1.6E-05	4.7E-04	2.0E-03	3.3E-03	1.4E-02	3.7E-03	1.6E-02	Y	Y
592-01-8	Cyanide	0	0	0.45	1.99	0	0	0.45	1.99	Y	Y
53-70-3	Dibenzo(a,h)anthracene	1.8E-07	7.7E-07	0	0	0	0	1.8E-07	7.7E-07	Y	Y
106-46-7	Dichlorobenzene	5.7E-05	2.3E-04	0	0	0	0	5.7E-05	2.3E-04	Y	Y
206-44-0	Fluoranthene	5.5E-06	7.0E-06	0	0	0	0	5.5E-06	7.0E-06	Y	N
86-73-7	Fluorene	1.7E-05	2.1E-05	0	0	0	0	1.7E-05	2.1E-05	Y	N
50-00-0	Formaldehyde	3.3E-03	1.5E-02	0	0	0	0	3.3E-03	1.5E-02	Y	Y
110-54-3	Hexane	8.5E-02	0.34	3.1E-02	0.14	0	0	0.12	0.48	Y	Y
7647-01-0	Hydrogen Chloride	0	0	0.99	3.67	0	0	0.99	**3.67**	Y	Y
193-39-5	Indeno(1,2,3-cd)pyrene	2.2E-07	9.6E-07	0	0	0	0	2.2E-07	9.6E-07	Y	Y
7439-92-1	Lead	0	0	4.8E-04	2.1E-03	6.5E-03	2.9E-02	7.0E-03	3.1E-02	Y	N
7439-96-5	Manganese	1.8E-05	7.2E-05	4.6E-03	1.7E-02	0.24	1.07	0.25	1.08	Y	Y
7439-97-6	Mercury	1.2E-05	5.0E-05	6.9E-04	2.9E-03	1.3E-03	5.7E-03	2.0E-03	8.6E-03	Y	N
91-20-3	Naphthalene	1.9E-04	3.1E-04	1.9E-03	8.5E-03	0	0	2.1E-03	8.8E-03	Y	Y
7440-02-0	Nickel	9.1E-05	4.0E-04	4.6E-04	2.0E-03	1.6E-03	7.1E-03	2.2E-03	9.5E-03	Y	Y
85-01-8	Phenanthrene	5.1E-05	6.3E-05	0	0	0	0	5.1E-05	6.3E-05	Y	N
108-95-2	Phenol	0	0	2.4E-04	1.1E-03	0	0	2.4E-04	1.1E-03	Y	Y
7723-14-0	Phosphorus	0	0	5.6E-03	2.3E-02	0.53	2.32	0.54	2.34	Y	Y
129-00-0	Pyrene	5.0E-06	6.6E-06	0	0	0	0	5.0E-06	6.6E-06	Y	N
7782-49-2	Selenium	1.1E-06	4.6E-06	4.1E-04	1.8E-03	3.3E-04	1.4E-03	7.4E-04	3.2E-03	Y	Y
108-88-3	Toluene	5.2E-04	1.1E-03	3.2E-02	0.14	0	0	3.2E-02	0.14	Y	Y
1330-20-7	Xylene	2.5E-04	3.0E-04	3.1E-02	0.14	0	0	3.2E-02	0.14	Y	Y
Total HAP		9.0E-02	0.36	1.58	6.25	1.36	5.95	3.03	12.56		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

	0.2155	0.8650	8.3307	31.6474	86.1858	377.4936	94.7319	410.0060
TRUE	0.2155	0.8650	8.3307	31.6474	86.1858	377.4936	94.7319	410.0060
	chk	chk	chk-15	chk	chk	chk	chk	chk

Hazardous Air Pollutants (HAP)/Toxic Air Pollutants (TAP) Emissions Summary - continued

		Emissions[1]									
		Fuel Combustion		Process/Prod/Leach		Mining		Total			
CAS	**Non-HAP TAP**	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	HAP	TAP
7429-90-5	Aluminum	0	0	0.65	2.58	57.86	253.41	58.50	255.98	N	Y
7440-39-3	Barium	2.1E-04	8.4E-04	6.6E-03	2.7E-02	0.65	2.86	0.66	2.88	N	Y
1317-65-3	Calcium Carbonate	0	0	2.24	8.12	11.41	49.97	13.65	58.09	N	Y
1305-78-8	Calcium Oxide	0	0	0.70	0.95	0	0	0.70	0.95	N	Y
7440-50-8	Copper	4.0E-05	1.6E-04	4.9E-04	2.1E-03	4.1E-03	1.8E-02	4.6E-03	2.0E-02	N	Y
110-82-7	Cyclohexane	0	0	1.0E-03	4.6E-03	0	0	1.0E-03	4.6E-03	N	Y
7783-06-4	Hydrogen Sulfide	0	0	0.90	3.94	0	0	0.90	3.94	N	Y
7439-89-6	Iron	0	0	0.21	0.81	14.83	64.96	15.04	65.77	N	Y
7439-98-7	Molybdenum	5.2E-05	2.1E-04	4.2E-04	1.8E-03	8.1E-04	3.6E-03	1.3E-03	5.6E-03	N	Y
109-66-0	Pentane	0.12	0.50	0	0	0	0	0.12	0.50	N	Y
7440-22-4	Silver	0	0	4.1E-04	1.8E-03	4.1E-04	1.8E-03	8.2E-04	3.6E-03	N	Y
7664-93-9	Sulfuric Acid	0	0	2.03	8.89	0	0	2.03	8.89	N	Y
7440-28-0	Thallium	0	0	5.2E-04	2.2E-03	8.1E-03	3.6E-02	8.7E-03	3.8E-02	N	Y
7440-61-1	Uranium	0	0	5.2E-04	2.2E-03	8.1E-03	3.6E-02	8.7E-03	3.8E-02	N	Y
7440-62-2	Vanadium	1.1E-04	4.4E-04	7.3E-04	3.0E-03	2.3E-02	1.0E-01	2.4E-02	0.10	N	Y
25551-13-7	Trimethyl benzene	0	0	1.1E-02	4.8E-02	0	0	1.1E-02	4.8E-02	N	Y
7440-33-7	Tungsten	0	0	5.2E-04	2.2E-03	8.1E-03	3.6E-02	8.7E-03	3.8E-02	N	Y
7440-66-6	Zinc	1.4E-03	5.5E-03	8.0E-04	3.3E-03	2.9E-02	0.12	3.1E-02	0.13	N	Y
Total Non-HAP TAP		0.13	0.50	6.75	25.40	84.83	371.54	91.71	397.44		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

Conversions

2,000 lb/ton
8,760 hr/yr
24 hr/day

PROPANE COMBUSTION

Source Data

Source ID	Description	MMBtu/day	MMBtu/yr
Lime Process Heating			
LKC	PFR Shaft Lime Kiln Combustion	529.0	163,935
Ore Process Heating			
ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	17.0	510
CKB	Carbon Regeneration Kiln (Burners)	54.1	19,754
PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	2.4	876
HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	120.0	43,800
Subtotal		193.5	64,940
HVAC			
H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	96.0	35,040
H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	96.0	35,040
HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	96.0	35,040
HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	12.0	4,380
HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	48.0	17,520
HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	72.0	26,280
Subtotal		438.0	159,870

PROPANE COMBUSTION - CONTINUED

HAP/TAP Emission Factors and Emissions

O.Heat_pph O.Heat_tpy L.Heat_pph L.Heat_tpy HVAC_pph HVAC_tpy lb/hr ton/yr

		Emission Factor[2]		Emissions[1] Ore Proc Heat		Lime Proc Heat		HVAC		Total			
CAS	Pollutant	lb/MMscf	lb/MMBtu[3]	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	TAP	A/C
91-57-6	2-Methylnaphthalene	2.4E-05	2.35E-8	1.9E-07	7.6E-07	5.2E-07	1.9E-06	4.3E-07	1.9E-06	1.1E-06	4.6E-06	N	
56-49-5	3-Methylchloranthrene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
57-97-6	7,12-Dimethylbenz(a)ant	< 1.6E-05	1.57E-8	1.3E-07	5.1E-07	3.5E-07	1.3E-06	2.9E-07	1.3E-06	7.6E-07	3.0E-06	N	
83-32-9	Acenaphthene	< 1.8E-06	1.76E-9	1.4E-08	5.7E-08	3.9E-08	1.4E-07	3.2E-08	1.4E-07	8.5E-08	3.4E-07	N	
208-96-8	Acenaphthylene	< 1.8E-06	1.76E-9	1.4E-08	5.7E-08	3.9E-08	1.4E-07	3.2E-08	1.4E-07	8.5E-08	3.4E-07	N	
120-12-7	Anthracene	< 2.4E-06	2.35E-9	1.9E-08	7.6E-08	5.2E-08	1.9E-07	4.3E-08	1.9E-07	1.1E-07	4.6E-07	N	
7440-38-2	Arsenic	2.0E-04	1.96E-7	1.5E-06	6.4E-06	3.7E-06	1.6E-05	3.6E-06	1.6E-05	8.7E-06	3.8E-05	Y	C
56-55-3	Benz(a)anthracene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
71-43-2	Benzene	2.1E-03	2.06E-6	1.5E-05	6.7E-05	3.9E-05	1.7E-04	3.8E-05	1.6E-04	9.1E-05	4.0E-04	Y	C
50-32-8	Benzo(a)pyrene	< 1.2E-06	1.18E-9	8.7E-09	3.8E-08	2.2E-08	9.6E-08	2.1E-08	9.4E-08	5.2E-08	2.3E-07	Y	C
205-99-2	Benzo(b)fluoranthene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
191-24-2	Benzo(g,h,i)perylene	< 1.2E-06	1.18E-9	9.5E-09	3.8E-08	2.6E-08	9.6E-08	2.1E-08	9.4E-08	5.7E-08	2.3E-07	N	
207-08-9	Benzo(k)fluoranthene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7440-41-7	Beryllium	< 1.2E-05	1.18E-8	8.7E-08	3.8E-07	2.2E-07	9.6E-07	2.1E-07	9.4E-07	5.2E-07	2.3E-06	Y	C
7440-43-9	Cadmium	1.1E-03	1.08E-6	8.0E-06	3.5E-05	2.0E-05	8.8E-05	2.0E-05	8.6E-05	4.8E-05	2.1E-04	Y	C
7440-47-3	Chromium	1.4E-03	1.37E-6	1.1E-05	4.5E-05	3.0E-05	1.1E-04	2.5E-05	1.1E-04	6.6E-05	2.7E-04	Y	A
218-01-9	Chrysene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7440-48-4	Cobalt	8.4E-05	8.24E-8	6.6E-07	2.7E-06	1.8E-06	6.8E-06	1.5E-06	6.6E-06	4.0E-06	1.6E-05	Y	A
53-70-3	Dibenzo(a,h)anthracene	< 1.2E-06	1.18E-9	8.7E-09	3.8E-08	2.2E-08	9.6E-08	2.1E-08	9.4E-08	5.2E-08	2.3E-07	Y	C
106-46-7	Dichlorobenzene	1.2E-03	1.18E-6	9.5E-06	3.8E-05	2.6E-05	9.6E-05	2.1E-05	9.4E-05	5.7E-05	2.3E-04	Y	A
206-44-0	Fluoranthene	3.0E-06	2.94E-9	2.4E-08	9.5E-08	6.5E-08	2.4E-07	5.4E-08	2.4E-07	1.4E-07	5.7E-07	N	
86-73-7	Fluorene	2.8E-06	2.75E-9	2.2E-08	8.9E-08	6.1E-08	2.3E-07	5.0E-08	2.2E-07	1.3E-07	5.3E-07	N	
50-00-0	Formaldehyde	7.5E-02	7.35E-5	5.5E-04	2.4E-03	1.4E-03	6.0E-03	1.3E-03	5.9E-03	3.3E-03	1.4E-02	Y	C
110-54-3	Hexane	1.8E+00	1.76E-3	1.4E-02	5.7E-02	3.9E-02	1.4E-01	3.2E-02	1.4E-01	8.5E-02	3.4E-01	Y	A
193-39-5	Indeno(1,2,3-cd)pyrene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7439-96-5	Manganese	3.8E-04	3.73E-7	3.0E-06	1.2E-05	8.2E-06	3.1E-05	6.8E-06	3.0E-05	1.8E-05	7.2E-05	Y	A
7439-97-6	Mercury	2.6E-04	2.55E-7	2.1E-06	8.3E-06	5.6E-06	2.1E-05	4.7E-06	2.0E-05	1.2E-05	5.0E-05	N	
91-20-3	Naphthalene	6.1E-04	5.98E-7	4.8E-06	1.9E-05	1.3E-05	4.9E-05	1.1E-05	4.8E-05	2.9E-05	1.2E-04	Y	A
7440-02-0	Nickel	2.1E-03	2.06E-6	1.5E-05	6.7E-05	3.9E-05	1.7E-04	3.8E-05	1.6E-04	9.1E-05	4.0E-04	Y	C
85-01-8	Phenanthrene	1.7E-05	1.67E-8	1.3E-07	5.4E-07	3.7E-07	1.4E-06	3.0E-07	1.3E-06	8.1E-07	3.2E-06	N	
129-00-0	Pyrene	5.0E-06	4.90E-9	4.0E-08	1.6E-07	1.1E-07	4.0E-07	8.9E-08	3.9E-07	2.4E-07	9.5E-07	N	
7782-49-2	Selenium	< 2.4E-05	2.35E-8	1.9E-07	7.6E-07	5.2E-07	1.9E-06	4.3E-07	1.9E-06	1.1E-06	4.6E-06	Y	A
108-88-3	Toluene	3.4E-03	3.33E-6	2.7E-05	1.1E-04	7.3E-05	2.7E-04	6.1E-05	2.7E-04	1.6E-04	6.5E-04	Y	A
109-66-0	Pentane	2.6E+00	2.55E-3	2.1E-02	8.3E-02	5.6E-02	2.1E-01	4.7E-02	2.0E-01	1.2E-01	5.0E-01	Y	A
7440-39-3	Barium	4.4E-03	4.31E-6	3.5E-05	1.4E-04	9.5E-05	3.5E-04	7.9E-05	3.4E-04	2.1E-04	8.4E-04	Y	A
7440-50-8	Copper	8.5E-04	8.33E-7	6.7E-06	2.7E-05	1.8E-05	6.8E-05	1.5E-05	6.7E-05	4.0E-05	1.6E-04	Y	A
7439-98-7	Molybdenum	1.1E-03	1.08E-6	8.7E-06	3.5E-05	2.4E-05	8.8E-05	2.0E-05	8.6E-05	5.2E-05	2.1E-04	Y	A
7440-62-2	Vanadium	2.3E-03	2.25E-6	1.8E-05	7.3E-05	5.0E-05	1.8E-04	4.1E-05	1.8E-04	1.1E-04	4.4E-04	Y	A
7440-66-6	Zinc	2.9E-02	2.84E-5	2.3E-04	9.2E-04	6.3E-04	2.3E-03	5.2E-04	2.3E-03	1.4E-03	5.5E-03	Y	A
Total				3.6E-02	1.4E-01	9.8E-02	3.6E-01	8.1E-02	3.5E-01	2.1E-01	8.6E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *AP-42, Table 1.4-3 & 1.4-4 (7/98) Natural Gas Combustion* 1.0766 1.0766

(3) *Natural Gas Higher Heating Value* 1,020 *MMBtu/MMscf* chk

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis	
	PROJECT NO: 335-20-3	PAGE: 5	OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021	

DIESEL COMBUSTION

Source Data

Source ID	Description	Power Rating kW	Power Rating hp	Operation hr/day	Operation hr/yr	Fuel Consumption[1] & [2] MMBtu/day	Fuel Consumption[1] & [2] MMBtu/yr
EDG1	Camp Emergency Generator	1,000	1,341	1	100	9.39	938.70
EDG2	Plant Emergency Generator #1	1,000	1,341	1	100	9.39	938.7
EDG3	Plant Emergency Generator #2	1,000	1,341	1	100	9.39	938.7
EDFP	Mill Fire Pump	200	268	1	100	1.88	187.7
Total						30.0	3,003.8

(1) *Based on brake specific fuel consumption for diesel generators* 7,000 *Btu/hp-hr* *AP-42 Tbl 3.3-1*

(2) *Heat Content of* 0.137 *MMBtu/gal* 1E+6 *Btu/MMBtu* 1.341 *hp/kW*

HAP/TAP Emission Factors and Emissions

lb/hr ton/yr

	Pollutant	Factor (lb/MMBtu) ≤600 hp[2]	Factor (lb/MMBtu) >600hp[3]	Emissions (≤600 hp) lb/hr	Emissions (≤600 hp) ton/yr	Emissions (>600 hp) lb/hr	Emissions (>600 hp) ton/yr	Total Emissions[1] lb/hr	Total Emissions[1] ton/yr	TAP	A/C
106-99-0	1,3-Butadiene	< 3.9E-05		8.4E-07	3.7E-06	0.0E+00	0.0E+00	8.4E-07	3.7E-06	Y	C
83-32-9	Acenaphthene	< 1.4E-06	4.7E-06	1.1E-07	1.3E-07	5.5E-06	6.6E-06	5.6E-06	6.7E-06	N	
208-96-8	Acenaphthylene	< 5.1E-06	9.2E-06	4.0E-07	4.7E-07	1.1E-05	1.3E-05	1.1E-05	1.3E-05	N	
75-07-0	Acetaldehyde	7.7E-04	2.5E-05	1.6E-05	7.2E-05	8.1E-06	3.5E-05	2.5E-05	1.1E-04	Y	C
107-02-8	Acrolein	< 9.3E-05	7.9E-06	7.2E-06	8.7E-06	9.2E-06	1.1E-05	1.6E-05	2.0E-05	Y	A
120-12-7	Anthracene	1.9E-06	1.2E-06	1.5E-07	1.8E-07	1.4E-06	1.7E-06	1.6E-06	1.9E-06	N	
56-55-3	Benz(a)anthracene	1.7E-06	6.2E-07	3.6E-08	1.6E-07	2.0E-07	8.8E-07	2.4E-07	1.0E-06	Y	C
71-43-2	Benzene	9.3E-04	7.8E-04	2.0E-05	8.8E-05	2.5E-04	1.1E-03	2.7E-04	1.2E-03	Y	C
50-32-8	Benzo(a)pyrene	< 1.9E-07	< 2.6E-07	4.0E-09	1.8E-08	8.3E-08	3.6E-07	8.7E-08	3.8E-07	Y	C
205-99-2	Benzo(b)fluoranthene	< 9.9E-08	< 1.1E-06	2.1E-09	9.3E-09	3.6E-07	1.6E-06	3.6E-07	1.6E-06	Y	C
191-24-2	Benzo(g,h,i)perylene	< 4.9E-07	< 5.6E-07	3.8E-08	4.6E-08	6.5E-07	7.8E-07	6.9E-07	8.3E-07	N	
207-08-9	Benzo(k)fluoranthene	< 1.6E-07	< 2.2E-07	3.3E-09	1.5E-08	7.0E-08	3.1E-07	7.3E-08	3.2E-07	Y	C
218-01-9	Chrysene	3.5E-07	1.5E-06	7.6E-09	3.3E-08	4.9E-07	2.2E-06	5.0E-07	2.2E-06	Y	C
53-70-3	Dibenzo(a,h)anthracene	< 5.8E-07	< 3.5E-07	1.2E-08	5.5E-08	1.1E-07	4.9E-07	1.2E-07	5.4E-07	Y	C
206-44-0	Fluoranthene	7.6E-06	4.0E-06	6.0E-07	7.1E-07	4.7E-06	5.7E-06	5.3E-06	6.4E-06	N	
86-73-7	Fluorene	2.9E-05	1.3E-05	2.3E-06	2.7E-06	1.5E-05	1.8E-05	1.7E-05	2.1E-05	N	
50-00-0	Formaldehyde	1.2E-03	7.9E-05	2.5E-05	1.1E-04	2.5E-05	1.1E-04	5.1E-05	2.2E-04	Y	C
193-39-5	Indeno(1,2,3-cd)pyrene	< 3.8E-07	< 4.1E-07	8.0E-09	3.5E-08	1.3E-07	5.8E-07	1.4E-07	6.2E-07	Y	C
91-20-3	Naphthalene	8.5E-05	1.3E-04	6.6E-06	8.0E-06	1.5E-04	1.8E-04	1.6E-04	1.9E-04	Y	A
85-01-8	Phenanthrene	2.9E-05	4.1E-05	2.3E-06	2.8E-06	4.8E-05	5.7E-05	5.0E-05	6.0E-05	N	
129-00-0	Pyrene	4.8E-06	3.7E-06	3.7E-07	4.5E-07	4.4E-06	5.2E-06	4.7E-06	5.7E-06	N	
108-88-3	Toluene	4.1E-04	2.8E-04	3.2E-05	3.8E-05	3.3E-04	4.0E-04	3.6E-04	4.3E-04	Y	A
1330-20-7	Xylene	2.9E-04	1.9E-04	2.2E-05	2.7E-05	2.3E-04	2.7E-04	2.5E-04	3.0E-04	Y	A
Total				1.4E-04	3.6E-04	1.1E-03	2.2E-03	1.2E-03	2.6E-03		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *AP-42, Tab. 3.3-2, 10/96, diesel engines (≤ 600 hp)* chk chk

(3) *AP-42, Tabs. 3.4-3 & 3.4-4, 10/96, large diesel engines (> 600 hp)*

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 6 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

ORE PROCESSING

Source Data

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
OC1	Loader Transfer of Ore to Grizzly	3.500	0.639
OC2	Grizzly to Apron Feeder	3.500	0.639
OC3	Apron Feeder to Dribble Conveyor	3.500	0.639
OC4	Apron Feeder to Vibrating Grizzly	3.500	0.639
OC5	Dribble Conveyor to Vibrating Grizzly	3.500	0.639
OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	3.500	0.639
OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	30.000	5.475
OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	3.500	0.639
OC9	Stockpile Transfers to Reclaim Conveyors	16.560	3.022
OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	16.560	3.022
OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	16.560	3.022
OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge C	33.120	6.044
OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	3.864	0.705
Total		141.164	25.762

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	667	3.9E-03	1.7E-02	Y	C
7440-41-7	Beryllium	3.2	1.9E-05	8.2E-05	Y	C
7440-43-9	Cadmium	0.50	2.9E-06	1.3E-05	Y	C
7440-48-4	Cobalt	4	2.4E-05	1.0E-04	Y	A
7440-47-3	Chromium	9	5.3E-05	2.3E-04	Y	A
7439-97-6	Mercury [3]	0.96	5.6E-06	2.5E-05	N	
7439-96-5	Manganese	299	1.8E-03	7.7E-03	Y	A
7440-02-0	Nickel	2	1.2E-05	5.2E-05	Y	C
7439-92-1	Lead	8	4.7E-05	2.1E-04	N	
7440-36-0	Antimony	23	1.4E-04	5.9E-04	Y	A
7723-14-0	Phosphorus	650	3.8E-03	1.7E-02	Y	A
7782-49-2	Selenium [4]	0.40	2.4E-06	1.0E-05	Y	A
7440-22-4	Silver	0.50	2.9E-06	1.3E-05	Y	A
7429-90-5	Aluminum	71,000	4.2E-01	1.8E+00	Y	A
7440-39-3	Barium	800	4.7E-03	2.1E-02	Y	A
1317-65-3	Calcium Carbonate	14,000	8.2E-02	3.6E-01	Y	A
7440-50-8	Copper	5	2.9E-05	1.3E-04	Y	A
7439-89-6	Iron [4]	18,200	1.1E-01	4.7E-01	Y	A
7439-98-7	Molybdenum	1	5.9E-06	2.6E-05	Y	A
7440-28-0	Thallium	10	5.9E-05	2.6E-04	Y	A
7440-61-1	Uranium	10	5.9E-05	2.6E-04	Y	A
7440-62-2	Vanadium	28	1.6E-04	7.2E-04	Y	A
7440-33-7	Tungsten	10	5.9E-05	2.6E-04	Y	A
7440-66-6	Zinc	35	2.1E-04	9.0E-04	Y	A
Total			6.2E-01	2.7E+00		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *(Midas Gold 2017c) Median concentration of 55,000 SGP samples.*

[3] *(Midas Gold 2018e) Median ore concentration of 151,000 SGP samples; resource block model.*

[4] *(Midas Gold 2020) Median concentration of 56,000 SGP samples for Fe and 1,500 SGP samples for Se.*

1E+6 parts/ppm

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 7 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

ORE CONCETRATION AND REFINING

Source Data

Source ID	Description	Subpart 7E Allowable Limit lb/yr[1]	Oper. hr/yr	% of Subpart 7E for Controlled Systems %		Controlled Hg Emissions lb/hr	ton/yr	lb/yr
AC	Autoclave	213.4	8,760	[2]		0.000023	0.00010	0.20
EW,MR,MF,CKD	Refinery Sources (C. Kiln, EW, Retort, Furn	16.8		20%	[3]	0.000384	0.00168	3.36
7439-97-6 Mercury	Total	230.2				0.000407	0.00178	3.56

[1] *Subpart 7E Limit - Ore Pretreatment Processes (CFR 2018b)*

$$\frac{84\ lb}{MMton} \times \frac{2{,}540{,}400\ ton}{yr} \times \frac{MMton}{1.0E+6\ ton} = \frac{213.4\ lb}{yr}$$

[1] *Subpart 7E Limit - Carbon Processes with Mercury Retorts*

$$\frac{0.8\ lb}{ton} \times \frac{21\ ton}{yr} = \frac{16.8\ lb}{yr}$$

[2] *Controlled SysCAD modeled emissions from Autoclave:* 0.0105 g/hr 2.3E-05 lb/hr 0.20 lb/yr (M3 2019)

[3] *Based on similar source (but with much higher ore Hg content) Hg reporting levels provided below:*

Goldstrike Refinery (2015 & 2016 Hg Reports) (NDEP 2015a) (NDEP 2016)

$$\frac{28.79\ lb}{yr} \times \frac{yr}{251.00\ ton} = \frac{0.11\ lb}{MMton} \times \frac{ton}{0.8\ lb} = 14.3\%$$

Twin Creeks Refinery (2015 & 2016 Hg Reports) (NDEP 2015a) (NDEP 2016)

$$\frac{31.27\ lb}{yr} \times \frac{yr}{142.77\ ton} = \frac{0.22\ lb}{MMton} \times \frac{ton}{0.8\ lb} = 27.4\%$$

HAP/TAP Emission Factors and Emission

AC_pph AC_tpy Refin_pph Refin_tpy lb/hr ton/yr

CAS No.	Pollutant	Emission Factor[1]	Autoclave lb/hr	Autoclave ton/yr	Refinery lb/hr	Refinery ton/yr	Total Emissions lb/hr	Total Emissions ton/yr	TAP	A/C
7440-38-2	Arsenic	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-41-7	Beryllium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-43-9	Cadmium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-48-4	Cobalt	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-47-3	Chromium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-97-6	Mercury	see above	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	N	
7439-96-5	Manganese	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-02-0	Nickel	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7439-92-1	Lead	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	N	
7440-36-0	Antimony	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7723-14-0	Phosphorus	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7782-49-2	Selenium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-22-4	Silver	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7429-90-5	Aluminum	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-39-3	Barium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
1317-65-3	Calcium Carbonate	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-50-8	Copper	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-89-6	Iron	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-98-7	Molybdenum	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-28-0	Thallium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-61-1	Uranium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-62-2	Vanadium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-33-7	Tungsten	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-66-6	Zinc	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
Total			5.5E-04	2.4E-03	9.2E-03	4.0E-02	9.8E-03	4.3E-02		

[1] *Hg is the most difficult metal to control due to it existing in both particulate and gaseous form. Therefore, all other metals are conservatively estimated to be equal to or less than the Hg emissions.*

0.0525 0.0525 chk

7664-93-9	Sulfuric Acid	Autoclave	2.03	8.89			2.03	8.89
7783-06-4	Hydrogen Sulfid	Autoclave	0.90	3.94			0.90	3.94
592-01-8	Cyanide	Point Sources - 5 EW Cells			0.0012	0.0053	0.00	0.01
Total			2.93	12.84	0.01	0.05	2.94	12.88

ORE CONCETRATION AND REFINING - CONTINUED

Source Data

Source ID	Description	Throughput ton/day	Throughput ton/yr	Operation hr/day	Operation hr/yr
AC	Autoclave	6,960	2,540,400	24	8,760

Autoclave HAP/TAP Emission Factors and Emission lb/hr ton/yr

CAS No.	Pollutant	Emission Factor		Emissions[1] lb/hr	Emissions[1] ton/yr
7664-93-9	Sulfuric Acid	0.007	lb/ton[2]	2.03	8.89
7783-06-4	Hydrogen Sulfide	0.9	lb/hr[3]	0.90	3.94

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *H2SO4 is based on Acidic Autoclave test data (APT 2010)*

[3] *H2S is based on Acidic Autoclave test data (APT 2013)*

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis	
	PROJECT NO: 335-20-3	PAGE: 9	OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021	

LEACHING OPERATION

Cyanide (HCN) Source Data, Emission Factors, and Emissions

Source ID	Description	Dia. ft[1]	pH[1]	Free CN- g/m3[1]	T C[1]	pKa	a0	H	kG[2] m/s	Fa*Fw	g/s	lb/hr	ton/yr
												lb/hr	ton/yr
TSF	***Fugitive Sources***												
TSF	Tailings Maint. Pond	76	7.75	1	3.74	9.803	0.9912	0.0025	1.89E-05	0.641	1.27E-05	0.0001	0.0004
MILLTA	CN Detox Tank 1	40	8.5	25	25	9.250	0.8490	0.0055	0.000311	0.688	0.002891	0.0229	0.101
MILLTA	CN Detox Tank 2	40	8.5	25	25	9.250	0.8490	0.0055	0.000311	0.688	0.002891	0.0229	0.101
MILLTA	CIP Leach Tank 1	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIP Leach Tank 2	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIP Leach Tank 3	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIP Leach Tank 4	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIL Tank 1	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 2	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 3	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 4	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 5	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 6	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIP Tank 1	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 2	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 3	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 4	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 5	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 6	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
		Acres[1]											
TSF	Tails, Aqueous Surface	110.222	7.75	1	3.74	9.803	0.9912	0.0025	1.89E-05	0.421	0.008845	0.0702	0.307
TSF	Tails, Wet Sediment	110.222							5.31E-08	0.421	0.009961	0.0791	0.346
TSF	Tails, Dry Sediment	110.222							2.33E-08	1	0.010375	0.0823	0.361
		330.666											
592-01-8	Cyanide Fugitive Sources - Subtotal											0.4527	1.983
75-15-0	Carbon Disulfide											0.01446	0.06332
	Point Sources												
EW	EW Cells	[3]										0.0006	0.003
EW	Preg/Barren Tanks	[3]										0.0006	0.003
592-01-8	Cyanide Point Sources - Subtotal											0.0012	0.0053
	Total											0.454	1.988

[1] *(Midas Gold 2016)(M3 2017c)(M3 2017d)*

[2] *The emission factors and caculation methodology are from the EPA directed HCN study: (Card, T. 2009)(EPA 2009)(Schmidt 2010)*

[3] *(APT 2009)*

Carbon Disulfide Emissions from Xanthate Decomposition

CAS No.	Pollutant	Xanthate[1] ton/yr	Molar Decomp.[2]	CS_2 MW Ratio	Temperature Adj. Factor[3]	Emissions lb/hr	Emissions ton/yr
75-15-0	Carbon Disulfide	1,700	0.99%	0.376	1%	0.0145	0.063

	MW	
Xanthate (PAX)	202.37	$C6H11KOS_2$
Carbon disulfide	76.139	CS_2

[1] *(Midas Gold 2016) p. 12-11*

[2] *(Air Sciences 2020) molar decomposition of xanthate in solution to CS2 gas*

[3] *(Air Sciences 2020) based on the comparison of CS2 generation at 25C and 70C*

Conversions

8,760	hr/yr	453.5929	g/lb
2,000	lb/ton	3.28084	ft/m
4,046.86	m2/acre	3,600	s/hr

Wind adjustment factor Fw 1

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis		
	PROJECT NO: 335-20-3	PAGE: 10	OF: 19	SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021		

LIME PRODUCTION

Source Data

Source ID	Description	Throughput ton/day	Throughput ton/yr	PM Emissions lb/day	PM Emissions ton/yr
LS1	Limestone transfer to Primary Crusher Hopper			3.39	0.48
LS2	Primary Crushing and Associated Transfers In and Out			6.10	0.86
LS3	Primary Screening and Associated Transfers In and Out			28.25	3.97
LS4	Secondary Crushing and Associated Transfers In and Out			6.10	0.86
LS5	Secondary Screening and Associated Transfers In and Out			28.25	3.97
LS6	Limestone transfer to Ball Mill Feed Bin			3.39	0.48
LS7	Limestone transfer to Ball Mill Feed Conveyor			3.39	0.48
LS8	Ball Mill Feed transfer to Ball Mill			3.39	0.48
LSBM	Limestone Ball Mill			45.65	6.42
LS9	Limestone transfer to Kiln Feed Bin			0.80	0.12
LS10	Limestone transfer to Lime Kiln Feed Conveyor			0.80	0.12
LS11	Fines Screening and Associated Transfers In and Out			6.68	1.03
Subtotal LS1-11				136.18	19.28
LS12	Kiln Feed transfer to PFR Shaft Lime Kiln			0.80	0.12
LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	169	52,377	21.97	3.40
Subtotal LS12,LK				22.77	3.53
Total				158.95	22.80

HAP/TAP Emission Factors and Emissions

			LS_pph	LS_tpy	LS12_pph	LS12_tpy	LK_pph	LK_tpy	lb/hr	ton/yr		
		Concentration	LS1-11,LSBM		LS12		Lime Kiln		Emissions[1]			
CAS No.	Pollutant	ppm[2]	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.01E-04	4.43E-04	6.51E-07	2.85E-06	1.79E-05	7.83E-05	1.20E-04	5.24E-04	Y	C
7440-41-7	Beryllium	0.8	3.52E-06	1.54E-05	2.27E-08	9.92E-08	6.22E-07	2.72E-06	4.17E-06	1.82E-05	Y	C
7440-43-9	Cadmium	0.25	1.10E-06	4.82E-06	7.08E-09	3.10E-08	1.94E-07	8.51E-07	1.30E-06	5.70E-06	Y	C
7440-48-4	Cobalt	4	2.27E-05	7.71E-05	1.34E-07	4.96E-07	3.66E-06	1.36E-05	2.65E-05	9.12E-05	Y	A
7440-47-3	Chromium	15	8.51E-05	2.89E-04	5.01E-07	1.86E-06	1.37E-05	5.11E-05	9.93E-05	3.42E-04	Y	A
7439-97-6	Mercury [3]	0.02	1.13E-07	3.86E-07	6.68E-10	2.48E-09	2.82E-04	1.05E-03	2.82E-04	1.05E-03	N	
7439-96-5	Manganese	236.5	1.34E-03	4.56E-03	7.89E-06	2.93E-05	2.16E-04	8.05E-04	1.57E-03	5.39E-03	Y	A
7440-02-0	Nickel	5	2.20E-05	9.64E-05	1.42E-07	6.20E-07	3.89E-06	1.70E-05	2.60E-05	1.14E-04	Y	C
7439-92-1	Lead	3	1.70E-05	5.78E-05	1.00E-07	3.72E-07	2.75E-06	1.02E-05	1.99E-05	6.84E-05	N	
7440-36-0	Antimony	2.5	1.42E-05	4.82E-05	8.34E-08	3.10E-07	2.29E-06	8.51E-06	1.66E-05	5.70E-05	Y	A
7723-14-0	Phosphorus	130	7.38E-04	2.51E-03	4.34E-06	1.61E-05	1.19E-04	4.43E-04	8.61E-04	2.96E-03	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	1.28E-01	4.36E-01	7.54E-04	2.80E-03	2.07E-02	7.69E-02	1.50E-01	5.15E-01	Y	A
7440-39-3	Barium	145	8.23E-04	2.79E-03	4.84E-06	1.80E-05	1.33E-04	4.94E-04	9.60E-04	3.31E-03	Y	A
1317-65-3	Calcium Carbonate	274500	1.56E+00	5.29E+00	9.16E-03	3.40E-02	2.51E-01	9.35E-01	1.82E+00	6.26E+00	Y	A
7440-50-8	Copper	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7439-89-6	Iron	10350	5.87E-02	1.99E-01	3.45E-04	1.28E-03	9.47E-03	3.52E-02	6.85E-02	2.36E-01	Y	A
7439-98-7	Molybdenum	0.5	2.84E-06	9.64E-06	1.67E-08	6.20E-08	4.58E-07	1.70E-06	3.31E-06	1.14E-05	Y	A
7440-28-0	Thallium	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-61-1	Uranium	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-62-2	Vanadium	15.5	8.79E-05	2.99E-04	5.17E-07	1.92E-06	1.42E-05	5.28E-05	1.03E-04	3.53E-04	Y	A
7440-33-7	Tungsten	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-66-6	Zinc	18	1.02E-04	3.47E-04	6.01E-07	2.23E-06	1.65E-05	6.13E-05	1.19E-04	4.10E-04	Y	A
Subtotal			1.75E+00	5.94E+00	1.03E-02	3.82E-02	2.82E-01	1.05E+00	2.04E+00	7.03E+00	9.0667	9.0667
7647-01-0	Hydrogen Chloride	0.14 lb/ton product[4]					0.99	3.67	0.99	3.67		chk

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *(M3 2018) Median concentrations of SGP limestone material. Metals with medians below the detection limit (DL) are set to 1/2DL.*

[3] *Hg emissions from the Lime Kiln are conservatively estimated assuming 100% volatilization of all Hg in the limestone*

[4] *(EPA 1999b)*

1E+6 parts/ppm

LIME PRODUCTION - CONTINUED

Source Data

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
LS1L	Mill Lime Silo #1 Loading	0.248	0.002
LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	1.200	0.011
MillS2L	Mill Lime Silo #2 Loading	0.248	0.002
MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	1.200	0.011
ACS1L	AC Lime Silo #1 Loading	0.990	0.009
ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.304	0.042
ACS2L	AC Lime Silo #2 Loading	0.990	0.009
ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.304	0.042
ACS3L	AC Lime Silo #3 Loading	0.990	0.009
ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.304	0.042
ACS4L	AC Lime Silo #4 Loading	0.495	0.004
ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	2.304	0.021
Subtotal - Mill & AC Lime Silos		15.576	0.203
LCR	Lime Mill Crushing and associated transfers In and Out	6.828	1.058
LSL	Pebble Lime Silo Loading via Bucket Elevator	0.149	0.023
LSU	Pebble Lime Silo discharge to Lime Slaker	0.015	0.002
Subtotal - Lime Mfg		6.991	1.083
Total		22.567	1.286

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Mill and AC lb/hr	Mill and AC ton/yr	Lime Mfg lb/hr	Lime Mfg ton/yr	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.06E-06	4.66E-06	5.69E-06	2.49E-05	6.75E-06	2.96E-05	Y	C
7440-41-7	Beryllium	0.8	3.70E-08	1.62E-07	1.98E-07	8.67E-07	2.35E-07	1.03E-06	Y	C
7440-43-9	Cadmium	0.25	1.16E-08	5.07E-08	6.18E-08	2.71E-07	7.34E-08	3.22E-07	Y	C
7440-48-4	Cobalt	4	2.60E-06	8.11E-07	1.17E-06	4.33E-06	3.76E-06	5.14E-06	Y	A
7440-47-3	Chromium	15	9.74E-06	3.04E-06	4.37E-06	1.63E-05	1.41E-05	1.93E-05	Y	A
7439-97-6	Mercury	0.02	1.30E-08	4.05E-09	5.83E-09	2.17E-08	1.88E-08	2.57E-08	N	
7439-96-5	Manganese	236.5	1.53E-04	4.79E-05	6.89E-05	2.56E-04	2.22E-04	3.04E-04	Y	A
7440-02-0	Nickel	5	2.31E-07	1.01E-06	1.24E-06	5.42E-06	1.47E-06	6.43E-06	Y	C
7439-92-1	Lead	3	1.95E-06	6.08E-07	8.74E-07	3.25E-06	2.82E-06	3.86E-06	N	
7440-36-0	Antimony	2.5	1.62E-06	5.07E-07	7.28E-07	2.71E-06	2.35E-06	3.22E-06	Y	A
7723-14-0	Phosphorus	130	8.44E-05	2.63E-05	3.79E-05	1.41E-04	1.22E-04	1.67E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22,600	1.47E-02	4.58E-03	6.58E-03	2.45E-02	2.13E-02	2.91E-02	Y	A
7440-39-3	Barium	145	9.41E-05	2.94E-05	4.22E-05	1.57E-04	1.36E-04	1.86E-04	Y	A
1305-78-8	Calcium Oxide	740,000 [3]	4.80E-01	1.50E-01	2.16E-01	8.02E-01	6.96E-01	9.52E-01	Y	A
7440-50-8	Copper	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7439-89-6	Iron	10350	6.72E-03	2.10E-03	3.01E-03	1.12E-02	9.73E-03	1.33E-02	Y	A
7439-98-7	Molybdenum	0.5	3.25E-07	1.01E-07	1.46E-07	5.42E-07	4.70E-07	6.43E-07	Y	A
7440-28-0	Thallium	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-61-1	Uranium	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-62-2	Vanadium	15.5	1.01E-05	3.14E-06	4.52E-06	1.68E-05	1.46E-05	1.99E-05	Y	A
7440-33-7	Tungsten	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-66-6	Zinc	18	1.17E-05	3.65E-06	5.24E-06	1.95E-05	1.69E-05	2.31E-05	Y	A
Total			5.02E-01	1.57E-01	2.25E-01	8.38E-01	7.27E-01	9.95E-01		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *See LIME PRODUCTION, page 10*

[3] *(NLA 2007) 40% to 74% CaO in lime*

1E+6 parts/ppm

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis		
	PROJECT NO: 335-20-3	PAGE: 12	OF: 19	SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021		

AGGREGATE PRODUCTION

Source Data

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conve	15.00	2.74
PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conve	15.00	2.74
Total		30.00	5.48

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	23	2.88E-05	1.26E-04	Y	C
7440-41-7	Beryllium	0.8	1.00E-06	4.38E-06	Y	C
7440-43-9	Cadmium	0.25	3.13E-07	1.37E-06	Y	C
7440-48-4	Cobalt	4	5.00E-06	2.19E-05	Y	A
7440-47-3	Chromium	15	1.88E-05	8.21E-05	Y	A
7439-97-6	Mercury	0.02	2.50E-08	1.10E-07	N	
7439-96-5	Manganese	236.5	2.96E-04	1.29E-03	Y	A
7440-02-0	Nickel	5	6.25E-06	2.74E-05	Y	C
7439-92-1	Lead	3	3.75E-06	1.64E-05	N	
7440-36-0	Antimony	2.5	3.13E-06	1.37E-05	Y	A
7723-14-0	Phosphorus	130	1.63E-04	7.12E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	2.83E-02	1.24E-01	Y	A
7440-39-3	Barium	145	1.81E-04	7.94E-04	Y	A
1317-65-3	Calcium Carbonate	274500	3.43E-01	1.50E+00	Y	A
7440-50-8	Copper	5	6.25E-06	2.74E-05	Y	A
7439-89-6	Iron	10350	1.29E-02	5.67E-02	Y	A
7439-98-7	Molybdenum	0.5	6.25E-07	2.74E-06	Y	A
7440-28-0	Thallium	5	6.25E-06	2.74E-05	Y	A
7440-61-1	Uranium	5	6.25E-06	2.74E-05	Y	A
7440-62-2	Vanadium	15.5	1.94E-05	8.49E-05	Y	A
7440-33-7	Tungsten	5	6.25E-06	2.74E-05	Y	A
7440-66-6	Zinc	18	2.25E-05	9.86E-05	Y	A
Total			3.85E-01	1.69E+00		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *See LIME PRODUCTION, page 10*

1E+6 parts/ppm

CONCRETE PRODUCTION

Source Data

TP_unit/day TP_unit/yr

Source ID	description Description	Throughput ton/day	ton/yr
CS1L	Cement/Shotcrete Silo #1 Loading	164	60,000
CS1U	Cement/Shotcrete Silo #1 Unloading	164	60,000
CS2L	Cement/Shotcrete Silo #2 Loading	164	60,000
CS2U	Cement/Shotcrete Silo #2 Unloading	164	60,000
CM	Central Mixer Loading	164	60,000
	Subtotal Cement Silo Filling	658	240,000
	Subtotal Central Mix Batching	164	60,000

HAP/TAP Emission Factors and Emissions

CF_pph CF_tpy CM_pph CM_tpy lb/hr ton/yr

CAS No.	HAP/TAP	Silo Fill lb/ton[2]	Central Mixer lb/ton[3]	Cement Silo L/U lb/hr	Cement Silo L/U ton/yr	Central Mix Batching lb/hr	Central Mix Batching ton/yr	Total Emissions[3] lb/hr	Total Emissions[3] ton/yr	TAP	A/C
7440-38-2	Arsenic	4.24E-09	2.96E-07	1.16E-7	5.09E-7	2.03E-6	8.88E-6	2.14E-6	9.39E-6	Y	C
7440-41-7	Beryllium	4.86E-10		1.33E-8	5.83E-8	--	--	1.33E-8	5.83E-8	Y	C
7440-43-9	Cadmium		7.10E-10	--	--	4.86E-9	2.13E-8	4.86E-9	2.13E-8	Y	C
7440-47-3	Chromium	2.90E-08	1.27E-07	7.95E-7	3.48E-6	8.70E-7	3.81E-6	1.66E-6	7.29E-6	Y	A
18540-29-9	Cr (VI)	5.80E-09	2.70E-08	1.59E-7	6.96E-7	1.85E-7	8.11E-7	3.44E-7	1.51E-6	Y	C
7439-92-1	Lead	1.09E-08	3.66E-08	2.99E-7	1.31E-6	2.51E-7	1.10E-6	5.49E-7	2.41E-6	N	
7439-96-5	Manganese	1.17E-07	3.78E-06	3.21E-6	1.40E-5	2.59E-5	1.13E-4	2.91E-5	1.27E-4	Y	A
7440-02-0	Nickel	4.18E-08	2.48E-07	1.15E-6	5.02E-6	1.70E-6	7.44E-6	2.84E-6	1.25E-5	Y	C
7723-14-0	Phosphorus		1.20E-06	--	--	8.22E-6	3.60E-5	8.22E-6	3.60E-5	Y	A
Total				5.73E-6	2.51E-5	3.91E-5	1.71E-4	4.49E-5	1.97E-4		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *AP-42, Table 11.12-8, (06/06) Cement Silo Filing, Controlled.* 20% *Cr (VI), IDEQ email on 11/23/2020* 0.0002 0.0002

(3) *AP-42, Table 11.12-8, (06/06) Central Mix Batching, Controlled.* 21.29% *Cr (VI), IDEQ email on 11/23/2020* chk

Conversions

24 hr/day

CONCRETE PRODUCTION - CONTINUED

Source Data

PM_ppd PM_tpy

Source ID	description Description	PM Emissions lb/day	ton/yr
CAL	Aggregate Bin Loading	16.56	1.73
CAU	Aggregate Bin Unloading	16.56	1.73
Total		33.12	3.45

HAP/TAP Emission Factors and Emissions

lb/hr ton/yr

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.81E-05	7.94E-05	Y	C
7440-41-7	Beryllium	0.8	6.30E-07	2.76E-06	Y	C
7440-43-9	Cadmium	0.25	1.97E-07	8.63E-07	Y	C
7440-48-4	Cobalt	4	5.52E-06	1.38E-05	Y	A
7440-47-3	Chromium	15	2.07E-05	5.18E-05	Y	A
7439-97-6	Mercury	0.02	2.76E-08	6.90E-08	N	
7439-96-5	Manganese	236.5	3.26E-04	8.16E-04	Y	A
7440-02-0	Nickel	5	3.94E-06	1.73E-05	Y	C
7439-92-1	Lead	3	4.14E-06	1.04E-05	N	
7440-36-0	Antimony	2.5	3.45E-06	8.63E-06	Y	A
7723-14-0	Phosphorus	130	1.79E-04	4.49E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	3.12E-02	7.80E-02	Y	A
7440-39-3	Barium	145	2.00E-04	5.00E-04	Y	A
7440-50-8	Copper	5	6.90E-06	1.73E-05	Y	A
7439-89-6	Iron	10350	1.43E-02	3.57E-02	Y	A
7439-98-7	Molybdenum	0.5	6.90E-07	1.73E-06	Y	A
7440-28-0	Thallium	5	6.90E-06	1.73E-05	Y	A
7440-61-1	Uranium	5	6.90E-06	1.73E-05	Y	A
7440-62-2	Vanadium	15.5	2.14E-05	5.35E-05	Y	A
7440-33-7	Tungsten	5	6.90E-06	1.73E-05	Y	A
7440-66-6	Zinc	18	2.48E-05	6.21E-05	Y	A
Total			4.63E-02	1.16E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *See LIME PRODUCTION, page 10*

1E+6 parts/ppm

FUEL STORAGE - GASOLINE

Source Data

Source ID	Description	VOC Emissions lb/day	VOC Emissions ton/yr
	description	VOC_ppd	VOC_tpy
TG1	Mine Site Gasoline Tank #1	5.25	0.96
TG2	Mine Site Gasoline Tank #2	5.25	0.96
Total		10.49	1.91

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration wt. %[2]	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
			lb/hr	ton/yr		
71-43-2	Benzene	1.608%	7.03E-03	3.08E-02	Y	C
92-52-4	Biphenyl	0.010%	4.37E-05	1.91E-04	Y	A
110-82-7	Cyclohexane	0.240%	1.05E-03	4.60E-03	Y	A
110-54-3	Hexane	7.138%	3.12E-02	1.37E-01	Y	A
91-20-3	Naphthalene	0.444%	1.94E-03	8.50E-03	Y	A
108-95-2	Phenol	0.055%	2.40E-04	1.05E-03	Y	A
108-88-3	Toluene	7.212%	3.15E-02	1.38E-01	Y	A
25551-13-7	Trimethyl benzene	2.500%	1.09E-02	4.79E-02	Y	A
1330-20-7	Xylene	7.170%	3.13E-02	1.37E-01	Y	A
Total			1.15E-01	5.05E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *(EPA 1999a)*

MINING FUGITIVE EMISSIONS

Dust Emissions

Source Data **Model Scenario** **W3** **180,000 T/day Emissions**

Operating schedule 365 day/yr

Clean rock cap (CR >0% [1]

[1] *(Perpetua 2021h) Percent of VMTs on haul roads capped with CR*
Roads outside of the pits and DRSFs are capped with CR

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
YPP	Yellow Pine Pit	--	--
HFP	Hangar Flats Pit	--	--
WEP	West End Pit	1,887.91	344.54
BT	Bradley Tailings	--	--
YPPBL	Yellow Pine Pit Blasting	--	--
HFPBL	Hangar Flats Pit Blasting	--	--
WEPBL	West End Pit Blasting	643.03	117.35
BTBL	Bradley Tailings Blasting	--	--
STKP	PC Stockpile	--	--
FDRSF	Fiddle DRSF	--	--
HFDRSF	Hangar Flats DRSF	289.91	52.91
YPDRSF	Yellow Pine DRSF	--	--
WEDRSF	West End DRSF	--	--
HR000	Haul Roads	16,697.74	3,047.34
TSF	Tailing Storage Facility	--	--
ACCRD	Access Roads	38.10	6.95
UGEXP	Scout Portal	0.008	0.002
Total		19,556.71	3,569.10

TSF, ACCRD, UGEXP 38.11 6.95 chk 3569.10

HAP/TAP Emission Factors		ORE	DR	CR	HRD	Borrow	AR
		Concentration					
CAS No.	Pollutant	ppm[1]	ppm[1]	ppm[3]	ppm[4]	ppm[5]	ppm
7440-38-2	Arsenic	667	667	90	667	2.5	667
7440-41-7	Beryllium	3.2	3.2		3.2		3.2
7440-43-9	Cadmium	0.5	0.5		0.5		0.5
7440-48-4	Cobalt	4	4		4		4
7440-47-3	Chromium	9	9		9		9
7439-97-6	Mercury [2]	0.96	0.6		0.6		0.6
7439-96-5	Manganese	299	299		299		299
7440-02-0	Nickel	2	2		2		2
7439-92-1	Lead	8	8		8		8
7440-36-0	Antimony	23	23		23		23
7723-14-0	Phosphorus	650	650		650		650
7782-49-2	Selenium	0.4	0.4		0.4		0.4
7440-22-4	Silver	0.5	0.5		0.5		0.5
7429-90-5	Aluminum	71000	71000		71000		71000
7440-39-3	Barium	800	800		800		800
1317-65-3	Calcium Carbonate	14000	14000		14000		14000
7440-50-8	Copper	5	5		5		5
7439-89-6	Iron	18200	18200		18200		18200
7439-98-7	Molybdenum	1	1		1		1
7440-28-0	Thallium	10	10		10		10
7440-61-1	Uranium	10	10		10		10
7440-62-2	Vanadium	28	28		28		28
7440-33-7	Tungsten	10	10		10		10
7440-66-6	Zinc	35	35		35		35

[1] *(Midas Gold 2017c)* *Median concentration of 55,000 SGP samples.* *1E+6 parts/ppm*

[2] *(Midas Gold 2018e)* *Median ore and development rock (DR) concentrations of 151,000 samples; resource block model.*

[3] *(Perpetua 2021g)* *Median concentration of 265 SGP samples.*

[4] *HRD: haul road - emissions calculated based on 0% of the total VMT occuring on CR*

[5] *(ALS 2018)* *Median concentration of 8 SGP samples.*

DR DR DR DR DR DR DR DR ORE DR DR DR DR HRD DR/AR

MINING FUGITIVE EMISSIONS - CONTINUED **Model Scenario W3** DR **180,000 T/day Emissions**

HAP/TAP Emissions

Hourly [1] YPP_pph HFP_pph WEP_pph BT_pph YPPBL_pph HFPBL_pph WEPBL_pph BTBL_pph STKP_pph FDRSF_pph HFDRSF_pph YPDRSF_pph WEDRSF_pph HR000_pph CCRD, UGE lb/hr

CAS No.	Pollutant	YPP lb/hr	HFP lb/hr	WEP lb/hr	BT lb/hr	YPPBL lb/hr	HFPBL lb/hr	WEPBL lb/hr	BTBL lb/hr	STKP lb/hr	FDRSF lb/hr	HFDRSF lb/hr	YPDRSF lb/hr	WEDRSF lb/hr	HR000 lb/hr	TSF, ACCRD, UGEXP lb/hr	Total lb/hr
7440-38-2	Arsenic	0	0	0.052	0	0	0	0.018	0	0	0	8.1E-3	0	0	0.464	1.1E-3	0.544
7440-41-7	Beryllium	0	0	2.5E-4	0	0	0	8.6E-5	0	0	0	3.9E-5	0	0	2.2E-3	5.1E-6	2.6E-3
7440-43-9	Cadmium	0	0	3.9E-5	0	0	0	1.3E-5	0	0	0	6.0E-6	0	0	3.5E-4	7.9E-7	4.1E-4
7440-48-4	Cobalt	0	0	3.1E-4	0	0	0	1.1E-4	0	0	0	4.8E-5	0	0	2.8E-3	6.4E-6	3.3E-3
7440-47-3	Chromium	0	0	7.1E-4	0	0	0	2.4E-4	0	0	0	1.1E-4	0	0	6.3E-3	1.4E-5	7.3E-3
7439-97-6	Mercury	0	0	4.7E-5	0	0	0	1.6E-5	0	0	0	7.2E-6	0	0	4.2E-4	9.5E-7	4.9E-4
7439-96-5	Manganese	0	0	0.024	0	0	0	8.0E-3	0	0	0	3.6E-3	0	0	0.208	4.7E-4	0.244
7440-02-0	Nickel	0	0	1.6E-4	0	0	0	5.4E-5	0	0	0	2.4E-5	0	0	1.4E-3	3.2E-6	1.6E-3
7439-92-1	Lead	0	0	6.3E-4	0	0	0	2.1E-4	0	0	0	9.7E-5	0	0	5.6E-3	1.3E-5	6.5E-3
7440-36-0	Antimony	0	0	1.8E-3	0	0	0	6.2E-4	0	0	0	2.8E-4	0	0	0.016	3.7E-5	0.019
7723-14-0	Phosphorus	0	0	0.051	0	0	0	0.017	0	0	0	7.9E-3	0	0	0.452	1.0E-3	0.530
7782-49-2	Selenium	0	0	3.1E-5	0	0	0	1.1E-5	0	0	0	4.8E-6	0	0	2.8E-4	6.4E-7	3.3E-4
7440-22-4	Silver	0	0	3.9E-5	0	0	0	1.3E-5	0	0	0	6.0E-6	0	0	3.5E-4	7.9E-7	4.1E-4
7429-90-5	Aluminum	0	0	5.585	0	0	0	1.902	0	0	0	0.858	0	0	49.397	0.113	57.855
7440-39-3	Barium	0	0	0.063	0	0	0	0.021	0	0	0	9.7E-3	0	0	0.557	1.3E-3	0.652
1317-65-3	Calcium Ca	0	0	1.101	0	0	0	0.375	0	0	0	0.169	0	0	9.740	0.022	11.408
7440-50-8	Copper	0	0	3.9E-4	0	0	0	1.3E-4	0	0	0	6.0E-5	0	0	3.5E-3	7.9E-6	4.1E-3
7439-89-6	Iron	0	0	1.432	0	0	0	0.488	0	0	0	0.220	0	0	12.662	0.029	14.831
7439-98-7	Molybdenu	0	0	7.9E-5	0	0	0	2.7E-5	0	0	0	1.2E-5	0	0	7.0E-4	1.6E-6	8.1E-4
7440-28-0	Thallium	0	0	7.9E-4	0	0	0	2.7E-4	0	0	0	1.2E-4	0	0	7.0E-3	1.6E-5	8.1E-3
7440-61-1	Uranium	0	0	7.9E-4	0	0	0	2.7E-4	0	0	0	1.2E-4	0	0	7.0E-3	1.6E-5	8.1E-3
7440-62-2	Vanadium	0	0	2.2E-3	0	0	0	7.5E-4	0	0	0	3.4E-4	0	0	0.019	4.4E-5	0.023
7440-33-7	Tungsten	0	0	7.9E-4	0	0	0	2.7E-4	0	0	0	1.2E-4	0	0	7.0E-3	1.6E-5	8.1E-3
7440-66-6	Zinc	0	0	2.8E-3	0	0	0	9.4E-4	0	0	0	4.2E-4	0	0	0.024	5.6E-5	0.029
Total		0	0	8.320	0	0	0	2.834	0	0	0	1.278	0	0	73.586	0.168	86.185

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.* chk 86.1849 86.1849

DR DR DR DR DR DR DR DR ORE DR DR DR DR HRD DR/AR

MINING FUGITIVE EMISSIONS - CONTINUED **Model Scenario W3** DR **180,000 T/day Emissions**

HAP/TAP Emissions

Annual

		YPP_tpy	HFP_tpy	WEP_tpy	BT_tpy	YPPBL_tpy	HFPBL_tpy	WEPBL_tpy	BTBL_tpy	STKP_tpy	FDRSF_tpy	HFDRSF_tpy	YPDRSF_tpy	WEDRSF_tpy	HR000_tpy	CCRD, UGE	ton/yr
		YPP	HFP	WEP	BT	YPPBL	HFPBL	WEPBL	BTBL	STKP	FDRSF	HFDRSF	YPDRSF	WEDRSF	HR000	TSF, ACCRD, UGEXP	Total
CAS No.	Pollutant	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr
7440-38-2	Arsenic	0	0	0.230	0	0	0	0.078	0	0	0	0.035	0	0	2.033	4.6E-3	2.381
7440-41-7	Beryllium	0	0	1.1E-3	0	0	0	3.8E-4	0	0	0	1.7E-4	0	0	9.8E-3	2.2E-5	0.011
7440-43-9	Cadmium	0	0	1.7E-4	0	0	0	5.9E-5	0	0	0	2.6E-5	0	0	1.5E-3	3.5E-6	1.8E-3
7440-48-4	Cobalt	0	0	1.4E-3	0	0	0	4.7E-4	0	0	0	2.1E-4	0	0	0.012	2.8E-5	0.014
7440-47-3	Chromium	0	0	3.1E-3	0	0	0	1.1E-3	0	0	0	4.8E-4	0	0	0.027	6.3E-5	0.032
7439-97-6	Mercury	0	0	2.1E-4	0	0	0	7.0E-5	0	0	0	3.2E-5	0	0	1.8E-3	4.2E-6	2.1E-3
7439-96-5	Manganese	0	0	0.103	0	0	0	0.035	0	0	0	0.016	0	0	0.911	2.1E-3	1.067
7440-02-0	Nickel	0	0	6.9E-4	0	0	0	2.3E-4	0	0	0	1.1E-4	0	0	6.1E-3	1.4E-5	7.1E-3
7439-92-1	Lead	0	0	2.8E-3	0	0	0	9.4E-4	0	0	0	4.2E-4	0	0	0.024	5.6E-5	0.029
7440-36-0	Antimony	0	0	7.9E-3	0	0	0	2.7E-3	0	0	0	1.2E-3	0	0	0.070	1.6E-4	0.082
7723-14-0	Phosphorus	0	0	0.224	0	0	0	0.076	0	0	0	0.034	0	0	1.981	4.5E-3	2.320
7782-49-2	Selenium	0	0	1.4E-4	0	0	0	4.7E-5	0	0	0	2.1E-5	0	0	1.2E-3	2.8E-6	1.4E-3
7440-22-4	Silver	0	0	1.7E-4	0	0	0	5.9E-5	0	0	0	2.6E-5	0	0	1.5E-3	3.5E-6	1.8E-3
7429-90-5	Aluminum	0	0	24.463	0	0	0	8.332	0	0	0	3.756	0	0	216	0.494	253
7440-39-3	Barium	0	0	0.276	0	0	0	0.094	0	0	0	0.042	0	0	2.438	5.6E-3	2.855
1317-65-3	Calcium Ca	0	0	4.824	0	0	0	1.643	0	0	0	0.741	0	0	42.663	0.097	49.967
7440-50-8	Copper	0	0	1.7E-3	0	0	0	5.9E-4	0	0	0	2.6E-4	0	0	0.015	3.5E-5	0.018
7439-89-6	Iron	0	0	6.271	0	0	0	2.136	0	0	0	0.963	0	0	55.462	0.127	64.958
7439-98-7	Molybdenu	0	0	3.4E-4	0	0	0	1.2E-4	0	0	0	5.3E-5	0	0	3.0E-3	7.0E-6	3.6E-3
7440-28-0	Thallium	0	0	3.4E-3	0	0	0	1.2E-3	0	0	0	5.3E-4	0	0	0.030	7.0E-5	0.036
7440-61-1	Uranium	0	0	3.4E-3	0	0	0	1.2E-3	0	0	0	5.3E-4	0	0	0.030	7.0E-5	0.036
7440-62-2	Vanadium	0	0	9.6E-3	0	0	0	3.3E-3	0	0	0	1.5E-3	0	0	0.085	1.9E-4	0.100
7440-33-7	Tungsten	0	0	3.4E-3	0	0	0	1.2E-3	0	0	0	5.3E-4	0	0	0.030	7.0E-5	0.036
7440-66-6	Zinc	0	0	0.012	0	0	0	4.1E-3	0	0	0	1.9E-3	0	0	0.107	2.4E-4	0.125
Total		0	0	36.441	0	0	0	12.412	0	0	0	5.596	0	0	322	0.736	377
															chk	377.4900	377.4900

MINING FUGITIVE EMISSIONS - CONTINUED

Mercury Evaporative Flux Emissions

Fugitive Mercury Flux and Emissions

			Area		Hg Flux	Emissions[1] lb/hr	ton/yr	lb/yr
CAS No.	Pollutant	Source	m^2	ha	µg/m^2-yr			
		Stockpiles	52,623	5.3	556	7.37E-6	3.2E-5	6.5E-2
		Rock Dumps	2,063,990	206.4	76.2	3.96E-5	1.7E-4	0.35
		Tailings	1,338,158	133.8	2,144	7.22E-4	3.2E-3	6.32
		Pits	1,504,919	150.5	132.3	5.01E-5	2.2E-4	0.44
7439-97-6	Mercury					8.2E-4	3.6E-3	7.17

[1] *Hourly emissions based on:* 8,760 *hours per year of operation*

Fugitive Mercury Emission Factors

	Twin Creeks (TC)		Ore Hg Adjusted	Stibnite	
	Hg Flux [1]	Hg [2]	µg/m^2/yr	Hg Flux [3]	Hg [4]
Source	µg/m^2-yr	µg/g	TC	µg/m^2-yr	µg/g
Stockpiles	5,609	33	556	556	0.96
Rock Dumps	768	3.5	76.2	76.2	0.60
Tailings	21,621	33	2,144	2,144	0.96
Pits	1,334	9.5	132	132.3	0.60

[1] *(Eckley 2010)* *Table 1: Hg flux µg/m^2-yr*

[2] *(Eckley 2010)* *Table 1: Average Hg flux mg/g: " Stockpiles - high-grade stockpiles, Rock Dumps - waste rock dumps, Tailings - high-grade stockpiles as a surrogate; Pits - pit"*

[3] *(Eckley 2010)* *Figure 2: log(y) = m*log(x) + b*

y = Hg Flux (ng/m^2-d)
x = material Hg concentration (µg/g)]

Slope =	*Solar*	*TC*
	Low	*0.59*
	Medium	*0.6*
	High	*0.77*
	Average	*0.65*

[4] *(Midas Gold 2018e)*

Sample Calculation: m = log (y1/y2) / log(x1/x2)

m=	0.65	unitless
y1=	5,609	µg/m^2-yr
x1=	33	µg/m^2-yr
x2=	0.96	µg/m^2-yr
log(x1/x2)=	1.536243	unitless
log(y1/y2)=	1.003679	unitless
y1/y2=	10.08506	unitless
y2=	556.2	µg/m^2-yr

Conversions

2,000	lb/ton
10,000	m2/ha
453.593	g/lb

TABLE A-W3. HAP/TAP Emissions and Exemptions

180,000 T/day Emissions						MINING										LEACHING	
chk						*Mining*	*Model Scenario*	*W3*								*CN Leach/PAX*	
						YPP,HFP,WEP,BT	YPPBL,HFPBL,WEPBL,BTBL		HR000		STKP, FDRSF, HFDRSF, YPDRSF, WEDRSF		TSF,ACCRD,UGEXP				
CAS	HAP/TAP	HAP	TAP			Pits		Blasting		Haul Roads		Stockpiles and DRFS		Tails, Access Road, Exploration		CN Leach and PAX	
	NSPS or NESHAP HAP/TAP -->			*Y*													
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
106-99-0	1,3-Butadiene	Y	Y	Y	C				0	0	0		0				
91-57-6	2-Methylnaphthalene	Y	N	n/a								0					
56-49-5	3-Methylchloranthrene	Y	Y	Y	C												
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a													
83-32-9	Acenaphthene	Y	N	n/a													
208-96-8	Acenaphthylene	Y	N	n/a													
75-07-0	Acetaldehyde	Y	Y	Y	C												
107-02-8	Acrolein	Y	Y	Y	A												
120-12-7	Anthracene	Y	N	n/a													
7440-36-0	Antimony	Y	Y	Y	A	1.8E-3	7.9E-3	6.2E-4	2.7E-3	0.016	0.070	2.8E-4	1.2E-3	3.7E-5	1.6E-4		
7440-38-2	Arsenic	Y	Y	Y	C	0.052	0.230	0.018	0.078	0.464	2.033	8.1E-3	0.035	1.1E-3	4.6E-3		
71-43-2	Benzene	Y	Y	Y	C												
50-32-8	Benzo(a)pyrene	Y	Y	Y	C												
56-55-3	Benz(a)anthracene	Y	Y	Y	C												
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C												
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C												
218-01-9	Chrysene	Y	Y	Y	C												
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C												
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C												
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a													
7440-41-7	Beryllium	Y	Y	Y	C	2.5E-4	1.1E-3	8.6E-5	3.8E-4	2.2E-3	9.8E-3	3.9E-5	1.7E-4	5.1E-6	2.2E-5		
92-52-4	Biphenyl	Y	Y	Y	A												
7440-43-9	Cadmium	Y	Y	Y	C	3.9E-5	1.7E-4	1.3E-5	5.9E-5	3.5E-4	1.5E-3	6.0E-6	2.6E-5	7.9E-7	3.5E-6		
75-15-0	Carbon Disulfide	Y	Y	Y	A											0.014	0.063
7440-47-3	Chromium	Y	Y	Y	A	7.1E-4	3.1E-3	2.4E-4	1.1E-3	6.3E-3	0.027	1.1E-4	4.8E-4	1.4E-5	6.3E-5		
18540-29-9	Cr (VI)	Y	Y	Y	C												
7440-48-4	Cobalt	Y	Y	Y	A	3.1E-4	1.4E-3	1.1E-4	4.7E-4	2.8E-3	0.012	4.8E-5	2.1E-4	6.4E-6	2.8E-5		
592-01-8	Cyanide	Y	Y	Y	A											0.453	1.983
106-46-7	Dichlorobenzene	Y	Y	Y	A												
206-44-0	Fluoranthene	Y	N	n/a													
86-73-7	Fluorene	Y	N	n/a													
50-00-0	Formaldehyde	Y	Y	Y	C												
110-54-3	Hexane	Y	Y	Y	A												
7647-01-0	Hydrogen Chloride	Y	Y	Y	A												
7439-92-1	Lead	Y	N	n/a		6.3E-4	2.8E-3	2.1E-4	9.4E-4	5.6E-3	0.024	9.7E-5	4.2E-4	1.3E-5	5.6E-5		
7439-96-5	Manganese	Y	Y	Y	A	0.024	0.103	8.0E-3	0.035	0.208	0.911	3.6E-3	0.016	4.7E-4	2.1E-3		
7439-97-6	Mercury	Y	N	n/a		9.7E-5	4.3E-4	1.6E-5	7.0E-5	4.2E-4	1.8E-3	5.4E-5	2.4E-4	7.2E-4	3.2E-3		
91-20-3	Naphthalene	Y	Y	Y	A												
7440-02-0	Nickel	Y	Y	Y	C	1.6E-4	6.9E-4	5.4E-5	2.3E-4	1.4E-3	6.1E-3	2.4E-5	1.1E-4	3.2E-6	1.4E-5		
85-01-8	Phenanthrene	Y	N	n/a													
108-95-2	Phenol	Y	Y	Y	A												
7723-14-0	Phosphorus	Y	Y	Y	A	0.051	0.224	0.017	0.076	0.452	1.981	7.9E-3	0.034	1.0E-3	4.5E-3		
129-00-0	Pyrene	Y	N	n/a													
7782-49-2	Selenium	Y	Y	Y	A	3.1E-5	1.4E-4	1.1E-5	4.7E-5	2.8E-4	1.2E-3	4.8E-6	2.1E-5	6.4E-7	2.8E-6		
108-88-3	Toluene	Y	Y	Y	A												
1330-20-7	Xylene	Y	Y	Y	A												
7429-90-5	Aluminum	N	Y	N	A	5.585	24.463	1.902	8.332	49.397	216	0.858	3.756	0.113	0.494		
7440-39-3	Barium	N	Y	N	A	0.063	0.276	0.021	0.094	0.557	2.438	9.7E-3	0.042	1.3E-3	5.6E-3		
1317-65-3	Calcium Carbonate	N	Y	N	A	1.101	4.824	0.375	1.643	9.740	42.663	0.169	0.741	0.022	0.097		
1305-78-8	Calcium Oxide	N	Y	N	A												
7440-50-8	Copper	N	Y	N	A	3.9E-4	1.7E-3	1.3E-4	5.9E-4	3.5E-3	0.015	6.0E-5	2.6E-4	7.9E-6	3.5E-5		
110-82-7	Cyclohexane	N	Y	N	A												
7783-06-4	Hydrogen Sulfide	N	Y	N	A												
7439-89-6	Iron	N	Y	N	A	1.432	6.271	0.488	2.136	12.662	55.462	0.220	0.963	0.029	0.127		
7439-98-7	Molybdenum	N	Y	N	A	7.9E-5	3.4E-4	2.7E-5	1.2E-4	7.0E-4	3.0E-3	1.2E-5	5.3E-5	1.6E-6	7.0E-6		
109-66-0	Pentane	N	Y	N	A												
7440-22-4	Silver	N	Y	N	A	3.9E-5	1.7E-4	1.3E-5	5.9E-5	3.5E-4	1.5E-3	6.0E-6	2.6E-5	7.9E-7	3.5E-6		
7664-93-9	Sulfuric Acid	N	Y	N	A												
7440-28-0	Thallium	N	Y	N	A	7.9E-4	3.4E-3	2.7E-4	1.2E-3	7.0E-3	0.030	1.2E-4	5.3E-4	1.6E-5	7.0E-5		
7440-61-1	Uranium	N	Y	N	A	7.9E-4	3.4E-3	2.7E-4	1.2E-3	7.0E-3	0.030	1.2E-4	5.3E-4	1.6E-5	7.0E-5		
7440-62-2	Vanadium	N	Y	N	A	2.2E-3	9.6E-3	7.5E-4	3.3E-3	0.019	0.085	3.4E-4	1.5E-3	4.4E-5	1.9E-4		
25551-13-7	Trimethyl benzene	N	Y	N	A												
7440-33-7	Tungsten	N	Y	N	A	7.9E-4	3.4E-3	2.7E-4	1.2E-3	7.0E-3	0.030	1.2E-4	5.3E-4	1.6E-5	7.0E-5		
7440-66-6	Zinc	N	Y	N	A	2.8E-3	0.012	9.4E-4	4.1E-3	0.024	0.107	4.2E-4	1.9E-3	5.6E-5	2.4E-4		
HAP TOTAL						***0.131***	***0.574***	***0.045***	***0.196***	***1.160***	***5.079***	***0.020***	***0.088***	***3.4E-3***	***0.015***	***0.467***	***2.046***
MERCURY TOTAL (exempt)						***9.7E-5***	***4.3E-4***	***1.6E-5***	***7.0E-5***	***4.2E-4***	***1.8E-3***	***5.4E-5***	***2.4E-4***	***7.2E-4***	***3.2E-3***		
MERCURY TOTAL (non-exempt)																	
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)																	
TAP TOTAL (For EL Evaluation)						***8.319***	***36.438***	***2.834***	***12.411***	***73.580***	***322***	***1.278***	***5.595***	***0.168***	***0.735***	***0.467***	***2.046***

TABLE A-W3. HAP/TAP Emissions and Exemptions

180,000 T/day Emissions						PROCESSING AND PRODUCTION											
chk						*Ore Processing*				*Ore Concentration and Refining*				*Process Heating*			
						OC1-13		PS		AC		EW,MR,MF,CKD		ACB, CKB, PV, HS		LKC	
CAS	HAP/TAP	HAP	TAP			Crushers & Xfers		Prill Silos		Autoclave		EW, Preg Tank, Retort, Furnace, Carbon Kiln		POX Boiler, C. Kiln Comb., Prop. Vap., Sol'n Heater		Lime Kiln Combustion	
	NSPS or NESHAP HAP/TAP -->			*Y*		*LL*	*LL*			*7E*	*7E*	*7E*	*7E*			*5A*	*5A*
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
106-99-0	1,3-Butadiene	Y	Y	Y	C												
91-57-6	2-Methylnaphthalene	Y	N	n/a										1.9E-7	7.6E-7	5.2E-7	1.9E-6
56-49-5	3-Methylchloranthrene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a										1.3E-7	5.1E-7	3.5E-7	1.3E-6
83-32-9	Acenaphthene	Y	N	n/a										1.4E-8	5.7E-8	3.9E-8	1.4E-7
208-96-8	Acenaphthylene	Y	N	n/a										1.4E-8	5.7E-8	3.9E-8	1.4E-7
75-07-0	Acetaldehyde	Y	Y	Y	C												
107-02-8	Acrolein	Y	Y	Y	A												
120-12-7	Anthracene	Y	N	n/a										1.9E-8	7.6E-8	5.2E-8	1.9E-7
7440-36-0	Antimony	Y	Y	Y	A	1.4E-4	5.9E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-38-2	Arsenic	Y	Y	Y	C	3.9E-3	0.017			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.5E-6	6.4E-6	3.7E-6	1.6E-5
71-43-2	Benzene	Y	Y	Y	C									1.5E-5	6.7E-5	3.9E-5	1.7E-4
50-32-8	Benzo(a)pyrene	Y	Y	Y	C									8.7E-9	3.8E-8	2.2E-8	9.6E-8
56-55-3	Benz(a)anthracene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
218-01-9	Chrysene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C									8.7E-9	3.8E-8	2.2E-8	9.6E-8
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a										9.5E-9	3.8E-8	2.6E-8	9.6E-8
7440-41-7	Beryllium	Y	Y	Y	C	1.9E-5	8.2E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.7E-8	3.8E-7	2.2E-7	9.6E-7
92-52-4	Biphenyl	Y	Y	Y	A												
7440-43-9	Cadmium	Y	Y	Y	C	2.9E-6	1.3E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.0E-6	3.5E-5	2.0E-5	8.8E-5
75-15-0	Carbon Disulfide	Y	Y	Y	A												
7440-47-3	Chromium	Y	Y	Y	A	5.3E-5	2.3E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.1E-5	4.5E-5	3.0E-5	1.1E-4
18540-29-9	Cr (VI)	Y	Y	Y	C												
7440-48-4	Cobalt	Y	Y	Y	A	2.4E-5	1.0E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	6.6E-7	2.7E-6	1.8E-6	6.8E-6
592-01-8	Cyanide	Y	Y	Y	A							1.2E-3	5.3E-3				
106-46-7	Dichlorobenzene	Y	Y	Y	A									9.5E-6	3.8E-5	2.6E-5	9.6E-5
206-44-0	Fluoranthene	Y	N	n/a										2.4E-8	9.5E-8	6.5E-8	2.4E-7
86-73-7	Fluorene	Y	N	n/a										2.2E-8	8.9E-8	6.1E-8	2.3E-7
50-00-0	Formaldehyde	Y	Y	Y	C									5.5E-4	2.4E-3	1.4E-3	6.0E-3
110-54-3	Hexane	Y	Y	Y	A									0.014	0.057	0.039	0.145
7647-01-0	Hydrogen Chloride	Y	Y	Y	A												
7439-92-1	Lead	Y	N	n/a		4.7E-5	2.1E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7439-96-5	Manganese	Y	Y	Y	A	1.8E-3	7.7E-3			2.3E-5	1.0E-4	3.8E-4	1.7E-3	3.0E-6	1.2E-5	8.2E-6	3.1E-5
7439-97-6	Mercury	Y	N	n/a		5.6E-6	2.5E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	2.1E-6	8.3E-6	5.6E-6	2.1E-5
91-20-3	Naphthalene	Y	Y	Y	A									4.8E-6	1.9E-5	1.3E-5	4.9E-5
7440-02-0	Nickel	Y	Y	Y	C	1.2E-5	5.2E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.5E-5	6.7E-5	3.9E-5	1.7E-4
85-01-8	Phenanthrene	Y	N	n/a										1.3E-7	5.4E-7	3.7E-7	1.4E-6
108-95-2	Phenol	Y	Y	Y	A												
7723-14-0	Phosphorus	Y	Y	Y	A	3.8E-3	0.017			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
129-00-0	Pyrene	Y	N	n/a										4.0E-8	1.6E-7	1.1E-7	4.0E-7
7782-49-2	Selenium	Y	Y	Y	A	2.4E-6	1.0E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.9E-7	7.6E-7	5.2E-7	1.9E-6
108-88-3	Toluene	Y	Y	Y	A									2.7E-5	1.1E-4	7.3E-5	2.7E-4
1330-20-7	Xylene	Y	Y	Y	A												
7429-90-5	Aluminum	N	Y	N	A	0.418	1.829			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-39-3	Barium	N	Y	N	A	4.7E-3	0.021			2.3E-5	1.0E-4	3.8E-4	1.7E-3	3.5E-5	1.4E-4	9.5E-5	3.5E-4
1317-65-3	Calcium Carbonate	N	Y	N	A	0.082	0.361			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
1305-78-8	Calcium Oxide	N	Y	N	A												
7440-50-8	Copper	N	Y	N	A	2.9E-5	1.3E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	6.7E-6	2.7E-5	1.8E-5	6.8E-5
110-82-7	Cyclohexane	N	Y	N	A												
7783-06-4	Hydrogen Sulfide	N	Y	N	A					0.900	3.942						
7439-89-6	Iron	N	Y	N	A	0.107	0.469			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7439-98-7	Molybdenum	N	Y	N	A	5.9E-6	2.6E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.7E-6	3.5E-5	2.4E-5	8.8E-5
109-66-0	Pentane	N	Y	N	A									0.021	0.083	0.056	0.209
7440-22-4	Silver	N	Y	N	A	2.9E-6	1.3E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7664-93-9	Sulfuric Acid	N	Y	N	A					2.030	8.891						
7440-28-0	Thallium	N	Y	N	A	5.9E-5	2.6E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-61-1	Uranium	N	Y	N	A	5.9E-5	2.6E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-62-2	Vanadium	N	Y	N	A	1.6E-4	7.2E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.8E-5	7.3E-5	5.0E-5	1.8E-4
25551-13-7	Trimethyl benzene	N	Y	N	A												
7440-33-7	Tungsten	N	Y	N	A	5.9E-5	2.6E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-66-6	Zinc	N	Y	N	A	2.1E-4	9.0E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	2.3E-4	9.2E-4	6.3E-4	2.3E-3
HAP TOTAL						***9.8E-3***	***0.043***			***2.8E-4***	***1.2E-3***	***5.8E-3***	***0.025***	***0.015***	***0.060***	***0.041***	***0.152***
MERCURY TOTAL (exempt)										***2.3E-5***	***1.0E-4***	***3.8E-4***	***1.7E-3***			***5.6E-6***	***2.1E-5***
MERCURY TOTAL (non-exempt)						***5.6E-6***	***2.5E-5***							***2.1E-6***	***8.3E-6***		
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)						***9.8E-3***	***0.043***			***2.3E-4***	***1.0E-3***	***5.0E-3***	***0.022***			***0.041***	***0.152***
TAP TOTAL (For EL Evaluation)						***0.612***	***2.682***			***2.930***	***12.835***	***4.6E-3***	***0.020***	***0.036***	***0.144***	***0.057***	***0.212***

TABLE A-W3. HAP/TAP Emissions and Exemptions

180,000 T/day Emissions

chk

CAS	HAP/TAP	HAP	TAP		
	NSPS or NESHAP HAP/TAP -->			*Y*	
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*
106-99-0	1,3-Butadiene	Y	Y	Y	C
91-57-6	2-Methylnaphthalene	Y	N	n/a	
56-49-5	3-Methylchloranthrene	Y	Y	Y	C
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a	
83-32-9	Acenaphthene	Y	N	n/a	
208-96-8	Acenaphthylene	Y	N	n/a	
75-07-0	Acetaldehyde	Y	Y	Y	C
107-02-8	Acrolein	Y	Y	Y	A
120-12-7	Anthracene	Y	N	n/a	
7440-36-0	Antimony	Y	Y	Y	A
7440-38-2	Arsenic	Y	Y	Y	C
71-43-2	Benzene	Y	Y	Y	C
50-32-8	Benzo(a)pyrene	Y	Y	Y	C
56-55-3	Benz(a)anthracene	Y	Y	Y	C
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C
218-01-9	Chrysene	Y	Y	Y	C
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a	
7440-41-7	Beryllium	Y	Y	Y	C
92-52-4	Biphenyl	Y	Y	Y	A
7440-43-9	Cadmium	Y	Y	Y	C
75-15-0	Carbon Disulfide	Y	Y	Y	A
7440-47-3	Chromium	Y	Y	Y	A
18540-29-9	Cr (VI)	Y	Y	Y	C
7440-48-4	Cobalt	Y	Y	Y	A
592-01-8	Cyanide	Y	Y	Y	A
106-46-7	Dichlorobenzene	Y	Y	Y	A
206-44-0	Fluoranthene	Y	N	n/a	
86-73-7	Fluorene	Y	N	n/a	
50-00-0	Formaldehyde	Y	Y	Y	C
110-54-3	Hexane	Y	Y	Y	A
7647-01-0	Hydrogen Chloride	Y	Y	Y	A
7439-92-1	Lead	Y	N	n/a	
7439-96-5	Manganese	Y	Y	Y	A
7439-97-6	Mercury	Y	N	n/a	
91-20-3	Naphthalene	Y	Y	Y	A
7440-02-0	Nickel	Y	Y	Y	C
85-01-8	Phenanthrene	Y	N	n/a	
108-95-2	Phenol	Y	Y	Y	A
7723-14-0	Phosphorus	Y	Y	Y	A
129-00-0	Pyrene	Y	N	n/a	
7782-49-2	Selenium	Y	Y	Y	A
108-88-3	Toluene	Y	Y	Y	A
1330-20-7	Xylene	Y	Y	Y	A
7429-90-5	Aluminum	N	Y	N	A
7440-39-3	Barium	N	Y	N	A
1317-65-3	Calcium Carbonate	N	Y	N	A
1305-78-8	Calcium Oxide	N	Y	N	A
7440-50-8	Copper	N	Y	N	A
110-82-7	Cyclohexane	N	Y	N	A
7783-06-4	Hydrogen Sulfide	N	Y	N	A
7439-89-6	Iron	N	Y	N	A
7439-98-7	Molybdenum	N	Y	N	A
109-66-0	Pentane	N	Y	N	A
7440-22-4	Silver	N	Y	N	A
7664-93-9	Sulfuric Acid	N	Y	N	A
7440-28-0	Thallium	N	Y	N	A
7440-61-1	Uranium	N	Y	N	A
7440-62-2	Vanadium	N	Y	N	A
25551-13-7	Trimethyl benzene	N	Y	N	A
7440-33-7	Tungsten	N	Y	N	A
7440-66-6	Zinc	N	Y	N	A
HAP TOTAL					
MERCURY TOTAL (exempt)					
MERCURY TOTAL (non-exempt)					
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)					
TAP TOTAL (For EL Evaluation)					

0	0	1	1	0	0	0	0	0	0	0	0	0	0

PROCESSING AND PRODUCTION - Continued

Lime Production						*Aggregate Prod.*		*Concrete Production*					
LS1-11,LSBM		LK,LS12,LCR,LS-L/U		LS1-L/U,MillS2-L/U,ACS1-4		PCSP1,PCSP2		CM		CS1L,CS1U,CS2L, CS2U		CA-L/U	
Limestone Crushers, Screens, Mill, Xfers		Lime Kiln, Kiln Feed, Lime Mill, Pebble Lime Silo		Lime Silos and Lime Mill Crushing		Portable Crushers, Screens, Xfers		Central Mixer		Cement Silo #1 and #2 L/U		Aggregate Bin	
OOO	*OOO*	*5A*	*5A*			*OOO*	*OOO*					*OOO*	*OOO*
lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
1.4E-5	4.8E-5	3.1E-6	1.2E-5	1.6E-6	5.1E-7	3.1E-6	1.4E-5					3.5E-6	8.6E-6
1.0E-4	4.4E-4	2.4E-5	1.1E-4	1.1E-6	4.7E-6	2.9E-5	1.3E-4	2.0E-6	8.9E-6	1.2E-7	5.1E-7	1.8E-5	7.9E-5
3.5E-6	1.5E-5	8.4E-7	3.7E-6	3.7E-8	1.6E-7	1.0E-6	4.4E-6			1.3E-8	5.8E-8	6.3E-7	2.8E-6
1.1E-6	4.8E-6	2.6E-7	1.2E-6	1.2E-8	5.1E-8	3.1E-7	1.4E-6	4.9E-9	2.1E-8			2.0E-7	8.6E-7
8.5E-5	2.9E-4	1.9E-5	6.9E-5	9.7E-6	3.0E-6	1.9E-5	8.2E-5	8.7E-7	3.8E-6	7.9E-7	3.5E-6	2.1E-5	5.2E-5
								1.9E-7	8.1E-7	1.6E-7	7.0E-7		
2.3E-5	7.7E-5	5.0E-6	1.8E-5	2.6E-6	8.1E-7	5.0E-6	2.2E-5					5.5E-6	1.4E-5
0	0	0.986	3.666										
1.7E-5	5.8E-5	3.7E-6	1.4E-5	1.9E-6	6.1E-7	3.8E-6	1.6E-5	2.5E-7	1.1E-6	3.0E-7	1.3E-6	4.1E-6	1.0E-5
1.3E-3	4.6E-3	2.9E-4	1.1E-3	1.5E-4	4.8E-5	3.0E-4	1.3E-3	2.6E-5	1.1E-4	3.2E-6	1.4E-5	3.3E-4	8.2E-4
1.1E-7	3.9E-7	2.8E-4	1.0E-3	1.3E-8	4.1E-9	2.5E-8	1.1E-7					2.8E-8	6.9E-8
2.2E-5	9.6E-5	5.3E-6	2.3E-5	2.3E-7	1.0E-6	6.3E-6	2.7E-5	1.7E-6	7.4E-6	1.1E-6	5.0E-6	3.9E-6	1.7E-5
7.4E-4	2.5E-3	1.6E-4	6.0E-4	8.4E-5	2.6E-5	1.6E-4	7.1E-4	8.2E-6	3.6E-5			1.8E-4	4.5E-4
0.128	0.436	0.028	0.104	0.015	4.6E-3	0.028	0.124					0.031	0.078
8.2E-4	2.8E-3	1.8E-4	6.7E-4	9.4E-5	2.9E-5	1.8E-4	7.9E-4					2.0E-4	5.0E-4
1.558	5.291	0.260	0.969			0.343	1.503						
		0.216	0.802	0.480	0.150								
2.8E-5	9.6E-5	6.2E-6	2.3E-5	3.2E-6	1.0E-6	6.3E-6	2.7E-5					6.9E-6	1.7E-5
0.059	0.199	0.013	0.048	6.7E-3	2.1E-3	0.013	0.057					0.014	0.036
2.8E-6	9.6E-6	6.2E-7	2.3E-6	3.2E-7	1.0E-7	6.3E-7	2.7E-6					6.9E-7	1.7E-6
0	0												
2.8E-5	9.6E-5	6.2E-6	2.3E-5	3.2E-6	1.0E-6	6.3E-6	2.7E-5					6.9E-6	1.7E-5
2.8E-5	9.6E-5	6.2E-6	2.3E-5	3.2E-6	1.0E-6	6.3E-6	2.7E-5					6.9E-6	1.7E-5
8.8E-5	3.0E-4	1.9E-5	7.1E-5	1.0E-5	3.1E-6	1.9E-5	8.5E-5					2.1E-5	5.3E-5
2.8E-5	9.6E-5	6.2E-6	2.3E-5	3.2E-6	1.0E-6	6.3E-6	2.7E-5					6.9E-6	1.7E-5
1.0E-4	3.5E-4	2.2E-5	8.3E-5	1.2E-5	3.6E-6	2.3E-5	9.9E-5					2.5E-5	6.2E-5
2.3E-3	***8.1E-3***	***0.987***	***3.669***	***2.6E-4***	***8.5E-5***	***5.3E-4***	***2.3E-3***	***3.9E-5***	***1.7E-4***	***5.7E-6***	***2.5E-5***	***5.6E-4***	***1.4E-3***
0	***0***	***2.8E-4***	***1.0E-3***										
1.1E-7	***3.9E-7***			***1.3E-8***	***4.1E-9***	***2.5E-8***	***1.1E-7***					***2.8E-8***	***6.9E-8***
2.3E-3	***8.0E-3***	***0.986***	***3.668***			***5.2E-4***	***2.3E-3***					***5.6E-4***	***1.4E-3***
1.746	***5.930***	***0.517***	***1.923***	***0.502***	***0.157***	***0.385***	***1.684***	***3.9E-5***	***1.7E-4***	***5.4E-6***	***2.4E-5***	***0.046***	***0.114***

TABLE A-W3. HAP/TAP Emissions and Exemptions

180,000 T/day Emissions						PROCESSING AND PRODUCTION - Continued						MINING and LEACHING - Totals									
chk						*HVAC*		*Emer. Power/Fire*		*Fuel Storage*		*HAP Total*		*Mercury Total*		*Mercury Total*		*TAP Total*		*TAP Total*	
						H1M,H2M,HM,HAC,HR,HA,HMO,HTS,HW		EDG1,EDG2,EDG3,EDFP		TG1,TG2				*Exempt*		*Non-Exempt*		*HAP-TAP addressed by NSPS/NESHAP*		*For EL Evaluation*	
CAS	HAP/TAP	HAP	TAP			Heaters		Emergency Generators and Fire Pump		Gasoline Fuel Tanks											
	NSPS or NESHAP HAP/TAP -->			*Y*				*4Z*	*4Z*	*6C*	*6C*										
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
106-99-0	1,3-Butadiene	Y	Y	Y	C			8.4E-7	3.7E-6			0	0					0	0	0	0
91-57-6	2-Methylnaphthalene	Y	N	n/a		4.3E-7	1.9E-6														
56-49-5	3-Methylchloranthrene	Y	Y	Y	C	3.2E-8	1.4E-7														
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a		2.9E-7	1.3E-6														
83-32-9	Acenaphthene	Y	N	n/a		3.2E-8	1.4E-7	5.6E-6	6.7E-6												
208-96-8	Acenaphthylene	Y	N	n/a		3.2E-8	1.4E-7	1.1E-5	1.3E-5												
75-07-0	Acetaldehyde	Y	Y	Y	C			2.5E-5	1.1E-4												
107-02-8	Acrolein	Y	Y	Y	A			1.6E-5	2.0E-5												
120-12-7	Anthracene	Y	N	n/a		4.3E-8	1.9E-7	1.6E-6	1.9E-6												
7440-36-0	Antimony	Y	Y	Y	A							0.019	0.082							0.019	0.082
7440-38-2	Arsenic	Y	Y	Y	C	3.6E-6	1.6E-5					0.544	2.381							0.544	2.381
71-43-2	Benzene	Y	Y	Y	C	3.8E-5	1.6E-4	2.7E-4	1.2E-3	7.0E-3	0.031										
50-32-8	Benzo(a)pyrene	Y	Y	Y	C	2.1E-8	9.4E-8	8.7E-8	3.8E-7												
56-55-3	Benz(a)anthracene	Y	Y	Y	C	3.2E-8	1.4E-7	2.4E-7	1.0E-6												
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C	3.2E-8	1.4E-7	3.6E-7	1.6E-6												
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C	3.2E-8	1.4E-7	7.3E-8	3.2E-7												
218-01-9	Chrysene	Y	Y	Y	C	3.2E-8	1.4E-7	5.0E-7	2.2E-6												
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C	2.1E-8	9.4E-8	1.2E-7	5.4E-7												
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C	3.2E-8	1.4E-7	1.4E-7	6.2E-7												
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a		2.1E-8	9.4E-8	6.9E-7	8.3E-7												
7440-41-7	Beryllium	Y	Y	Y	C	2.1E-7	9.4E-7					2.6E-3	0.011							2.6E-3	0.011
92-52-4	Biphenyl	Y	Y	Y	A					4.4E-5	1.9E-4										
7440-43-9	Cadmium	Y	Y	Y	C	2.0E-5	8.6E-5					4.1E-4	1.8E-3							4.1E-4	1.8E-3
75-15-0	Carbon Disulfide	Y	Y	Y	A							0.014	0.063							0.014	0.063
7440-47-3	Chromium	Y	Y	Y	A	2.5E-5	1.1E-4					7.3E-3	0.032							7.3E-3	0.032
18540-29-9	Cr (VI)	Y	Y	Y	C																
7440-48-4	Cobalt	Y	Y	Y	A	1.5E-6	6.6E-6					3.3E-3	0.014							3.3E-3	0.014
592-01-8	Cyanide	Y	Y	Y	A							0.453	1.983							0.453	1.983
106-46-7	Dichlorobenzene	Y	Y	Y	A	2.1E-5	9.4E-5														
206-44-0	Fluoranthene	Y	N	n/a		5.4E-8	2.4E-7	5.3E-6	6.4E-6												
86-73-7	Fluorene	Y	N	n/a		5.0E-8	2.2E-7	1.7E-5	2.1E-5												
50-00-0	Formaldehyde	Y	Y	Y	C	1.3E-3	5.9E-3	5.1E-5	2.2E-4												
110-54-3	Hexane	Y	Y	Y	A	0.032	0.141			0.031	0.137										
7647-01-0	Hydrogen Chloride	Y	Y	Y	A																
7439-92-1	Lead	Y	N	n/a								6.5E-3	0.029								
7439-96-5	Manganese	Y	Y	Y	A	6.8E-6	3.0E-5					0.244	1.067							0.244	1.067
7439-97-6	Mercury	Y	N	n/a		4.7E-6	2.0E-5					1.3E-3	5.7E-3	1.3E-3	5.7E-3	0	0	0	0	0	0
91-20-3	Naphthalene	Y	Y	Y	A	1.1E-5	4.8E-5	1.6E-4	1.9E-4	1.9E-3	8.5E-3	0	0					0	0	0	0
7440-02-0	Nickel	Y	Y	Y	C	3.8E-5	1.6E-4					1.6E-3	7.1E-3					0	0	1.6E-3	7.1E-3
85-01-8	Phenanthrene	Y	N	n/a		3.0E-7	1.3E-6	5.0E-5	6.0E-5			0	0					0	0	0	0
108-95-2	Phenol	Y	Y	Y	A					2.4E-4	1.1E-3	0	0					0	0	0	0
7723-14-0	Phosphorus	Y	Y	Y	A							0.530	2.320					0	0	0.530	2.320
129-00-0	Pyrene	Y	N	n/a		8.9E-8	3.9E-7	4.7E-6	5.7E-6			0	0					0	0	0	0
7782-49-2	Selenium	Y	Y	Y	A	4.3E-7	1.9E-6					3.3E-4	1.4E-3					0	0	3.3E-4	1.4E-3
108-88-3	Toluene	Y	Y	Y	A	6.1E-5	2.7E-4	3.6E-4	4.3E-4	0.032	0.138	0	0					0	0	0	0
1330-20-7	Xylene	Y	Y	Y	A			2.5E-4	3.0E-4	0.031	0.137	0	0					0	0	0	0
7429-90-5	Aluminum	N	Y	N	A							0	0					0	0	57.855	253
7440-39-3	Barium	N	Y	N	A	7.9E-5	3.4E-4					0	0					0	0	0.652	2.855
1317-65-3	Calcium Carbonate	N	Y	N	A							0	0					0	0	11.408	49.967
1305-78-8	Calcium Oxide	N	Y	N	A							0	0					0	0	0	0
7440-50-8	Copper	N	Y	N	A	1.5E-5	6.7E-5					0	0					0	0	4.1E-3	0.018
110-82-7	Cyclohexane	N	Y	N	A					1.0E-3	4.6E-3	0	0					0	0	0	0
7783-06-4	Hydrogen Sulfide	N	Y	N	A							0	0					0	0	0	0
7439-89-6	Iron	N	Y	N	A							0	0					0	0	14.831	64.958
7439-98-7	Molybdenum	N	Y	N	A	2.0E-5	8.6E-5					0	0					0	0	8.1E-4	3.6E-3
109-66-0	Pentane	N	Y	N	A	0.047	0.204					0	0					0	0	0	0
7440-22-4	Silver	N	Y	N	A							0	0					0	0	4.1E-4	1.8E-3
7664-93-9	Sulfuric Acid	N	Y	N	A							0	0					0	0	0	0
7440-28-0	Thallium	N	Y	N	A							0	0					0	0	8.1E-3	0.036
7440-61-1	Uranium	N	Y	N	A							0	0					0	0	8.1E-3	0.036
7440-62-2	Vanadium	N	Y	N	A	4.1E-5	1.8E-4					0	0					0	0	0.023	0.100
25551-13-7	Trimethyl benzene	N	Y	N	A					0.011	0.048	0	0					0	0	0	0
7440-33-7	Tungsten	N	Y	N	A							0	0					0	0	8.1E-3	0.036
7440-66-6	Zinc	N	Y	N	A	5.2E-4	2.3E-3					0	0					0	0	0.029	0.125
HAP TOTAL						***0.034***	***0.148***	***1.2E-3***	***2.6E-3***	***0.103***	***0.453***	***1.826***	***7.998***								
MERCURY TOTAL (exempt)														***1.3E-3***	***5.7E-3***						
MERCURY TOTAL (non-exempt)						***4.7E-6***	***2.0E-5***									***0***	***0***				
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)								***1.1E-3***	***2.5E-3***	***0.103***	***0.453***							***0***	***0***		
TAP TOTAL (For EL Evaluation)						***0.081***	***0.355***			***0.012***	***0.052***									***86.645***	***380***

TABLE A-W3. HAP/TAP Emissions and Exemptions

180,000 T/day Emissions						PROCESSING AND PRODUCTION - Totals										ALL	ALL	ALL	TAP EL	
chk						*HAP Total*		*Mercury Total Exempt*		*Mercury Total Non-Exempt*		*TAP Total HAP-TAP addressed by NSPS/NESHAP*		*TAP Total For EL Evaluation*		*HAP*	*Hg Non-Exempt*	*TAP For EL Evaluation*	*TAP Emission Screening Level (EL)*	
CAS	HAP/TAP	HAP	TAP																	
	NSPS or NESHAP HAP/TAP -->			*Y*															Non-car	Carcin
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	ton/yr	ton/yr	lb/hr	lb/hr	lb/hr
106-99-0	1,3-Butadiene	Y	Y	Y	C	8.4E-7	3.7E-6					8.4E-7	3.7E-6			3.7E-6		0	--	2.4E-5
91-57-6	2-Methylnaphthalene	Y	N	n/a		1.1E-6	4.6E-6									4.6E-6			--	--
56-49-5	3-Methylchloranthrene	Y	Y	Y	C	7.8E-8	3.4E-7					3.3E-8	1.4E-7	4.5E-8	2.0E-7	3.4E-7		4.5E-8	--	2.5E-6
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a		7.6E-7	3.0E-6									3.0E-6			--	--
83-32-9	Acenaphthene	Y	N	n/a		5.7E-6	7.1E-6									7.1E-6			--	--
208-96-8	Acenaphthylene	Y	N	n/a		1.1E-5	1.4E-5									1.4E-5			--	--
75-07-0	Acetaldehyde	Y	Y	Y	C	2.5E-5	1.1E-4					2.5E-5	1.1E-4			1.1E-4			--	3.0E-3
107-02-8	Acrolein	Y	Y	Y	A	1.6E-5	2.0E-5					1.6E-5	2.0E-5			2.0E-5			0.017	--
120-12-7	Anthracene	Y	N	n/a		1.7E-6	2.4E-6									2.4E-6			--	--
7440-36-0	Antimony	Y	Y	Y	A	5.7E-4	2.5E-3					5.7E-4	2.5E-3	1.6E-6	5.1E-7	0.085		0.019	0.033	--
7440-38-2	Arsenic	Y	Y	Y	C	4.5E-3	0.020					4.5E-3	0.020	8.2E-6	3.6E-5	2.400		0.544	--	1.5E-6
71-43-2	Benzene	Y	Y	Y	C	7.4E-3	0.032					7.3E-3	0.032	5.3E-5	2.3E-4	0.032		5.3E-5	--	8.0E-4
50-32-8	Benzo(a)pyrene	Y	Y	Y	C	1.4E-7	6.1E-7					1.1E-7	4.8E-7	3.0E-8	1.3E-7	6.1E-7				
56-55-3	Benz(a)anthracene	Y	Y	Y	C	3.1E-7	1.4E-6					2.7E-7	1.2E-6	4.5E-8	2.0E-7	1.4E-6				
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C	4.4E-7	1.9E-6					3.9E-7	1.7E-6	4.5E-8	2.0E-7	1.9E-6				
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C	1.5E-7	6.6E-7					1.1E-7	4.7E-7	4.5E-8	2.0E-7	6.6E-7		2.9E-7	--	2.0E-6
218-01-9	Chrysene	Y	Y	Y	C	5.8E-7	2.5E-6					5.3E-7	2.3E-6	4.5E-8	2.0E-7	2.5E-6				
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C	1.8E-7	7.7E-7					1.5E-7	6.4E-7	3.0E-8	1.3E-7	7.7E-7				
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C	2.2E-7	9.6E-7					1.7E-7	7.6E-7	4.5E-8	2.0E-7	9.6E-7				
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a		7.5E-7	1.1E-6									1.1E-6			--	--
7440-41-7	Beryllium	Y	Y	Y	C	4.3E-4	1.9E-3					4.3E-4	1.9E-3	3.5E-7	1.5E-6	0.013		2.6E-3	--	2.8E-5
92-52-4	Biphenyl	Y	Y	Y	A	4.4E-5	1.9E-4					4.4E-5	1.9E-4			1.9E-4			0.100	--
7440-43-9	Cadmium	Y	Y	Y	C	4.6E-4	2.0E-3					4.3E-4	1.9E-3	2.8E-5	1.2E-4	3.8E-3		4.4E-4	--	3.7E-6
75-15-0	Carbon Disulfide	Y	Y	Y	A											0.063		0.014	2.000	--
7440-47-3	Chromium	Y	Y	Y	A	6.8E-4	2.8E-3					6.3E-4	2.6E-3	4.8E-5	1.6E-4	0.035		7.4E-3	0.033	--
18540-29-9	Cr (VI)	Y	Y	Y	C	3.4E-7	1.5E-6							3.4E-7	1.5E-6	1.5E-6		3.4E-7	--	5.6E-7
7440-48-4	Cobalt	Y	Y	Y	A	4.7E-4	2.0E-3					4.7E-4	2.0E-3	4.8E-6	1.0E-5	0.016		3.3E-3	3.3E-3	--
592-01-8	Cyanide	Y	Y	Y	A	1.2E-3	5.3E-3					1.2E-3	5.3E-3			1.988		0.453	0.333	--
106-46-7	Dichlorobenzene	Y	Y	Y	A	5.7E-5	2.3E-4					2.6E-5	9.6E-5	3.1E-5	1.3E-4	2.3E-4		3.1E-5	30.000	--
206-44-0	Fluoranthene	Y	N	n/a		5.5E-6	7.0E-6									7.0E-6			--	--
86-73-7	Fluorene	Y	N	n/a		1.7E-5	2.1E-5									2.1E-5			--	--
50-00-0	Formaldehyde	Y	Y	Y	C	3.3E-3	0.015					1.4E-3	6.2E-3	1.9E-3	8.3E-3	0.015		1.9E-3	--	5.1E-4
110-54-3	Hexane	Y	Y	Y	A	0.117	0.480					0.070	0.281	0.046	0.198	0.480		0.046	12.000	--
7647-01-0	Hydrogen Chloride	Y	Y	Y	A	0.986	3.666					0.986	3.666			3.666			0.050	--
7439-92-1	Lead	Y	N	n/a		4.8E-4	2.1E-3									0.031			--	--
7439-96-5	Manganese	Y	Y	Y	A	4.6E-3	0.017					4.4E-3	0.017	1.9E-4	2.2E-4	1.085		0.244	0.067	--
7439-97-6	Mercury	Y	N	n/a		7.1E-4	2.9E-3	6.9E-4	2.8E-3	1.3E-5	5.4E-5					8.6E-3	5.4E-5		--	--
91-20-3	Naphthalene	Y	Y	Y	A	2.1E-3	8.8E-3					2.1E-3	8.7E-3	1.6E-5	6.7E-5	8.8E-3		1.6E-5	3.330	--
7440-02-0	Nickel	Y	Y	Y	C	5.5E-4	2.4E-3					4.9E-4	2.2E-3	5.6E-5	2.4E-4	9.5E-3		1.7E-3	--	2.7E-5
85-01-8	Phenanthrene	Y	N	n/a		5.1E-5	6.3E-5									6.3E-5			--	--
108-95-2	Phenol	Y	Y	Y	A	2.4E-4	1.1E-3					2.4E-4	1.1E-3			1.1E-3			1.270	--
7723-14-0	Phosphorus	Y	Y	Y	A	5.6E-3	0.023					5.5E-3	0.023	9.3E-5	6.2E-5	2.343		0.530	7.0E-3	--
129-00-0	Pyrene	Y	N	n/a		5.0E-6	6.6E-6									6.6E-6			--	--
7782-49-2	Selenium	Y	Y	Y	A	4.1E-4	1.8E-3					4.1E-4	1.8E-3	6.2E-7	2.6E-6	3.2E-3		3.3E-4	0.013	--
108-88-3	Toluene	Y	Y	Y	A	0.032	0.139					0.032	0.139	8.8E-5	3.7E-4	0.139		8.8E-5	25.000	--
1330-20-7	Xylene	Y	Y	Y	A	0.032	0.138					0.032	0.138			0.138			29.000	--
7429-90-5	Aluminum	N	Y	N	A									0.648	2.577			58.504	0.667	--
7440-39-3	Barium	N	Y	N	A									6.8E-3	0.028			0.659	0.033	--
1317-65-3	Calcium Carbonate	N	Y	N	A									2.244	8.125			13.652	0.667	--
1305-78-8	Calcium Oxide	N	Y	N	A									0.696	0.952			0.696	0.133	--
7440-50-8	Copper	N	Y	N	A									5.3E-4	2.2E-3			4.6E-3	0.067	--
110-82-7	Cyclohexane	N	Y	N	A									1.0E-3	4.6E-3			1.0E-3	70.000	--
7783-06-4	Hydrogen Sulfide	N	Y	N	A									0.900	3.942			0.900	0.933	--
7439-89-6	Iron	N	Y	N	A									0.213	0.812			15.043	0.067	--
7439-98-7	Molybdenum	N	Y	N	A									4.7E-4	2.0E-3			1.3E-3	0.333	--
109-66-0	Pentane	N	Y	N	A									0.123	0.495			0.123	118	--
7440-22-4	Silver	N	Y	N	A									4.1E-4	1.8E-3			8.2E-4	7.0E-3	--
7664-93-9	Sulfuric Acid	N	Y	N	A									2.030	8.891			2.030	0.067	--
7440-28-0	Thallium	N	Y	N	A									5.2E-4	2.2E-3			8.7E-3	7.0E-3	--
7440-61-1	Uranium	N	Y	N	A									5.2E-4	2.2E-3			8.7E-3	0.013	--
7440-62-2	Vanadium	N	Y	N	A									8.4E-4	3.5E-3			0.024	3.0E-3	--
25551-13-7	Trimethyl benzene	N	Y	N	A									0.011	0.048			0.011	8.200	--
7440-33-7	Tungsten	N	Y	N	A									5.2E-4	2.2E-3	0		8.7E-3	0.333	--
7440-66-6	Zinc	N	Y	N	A									2.2E-3	8.8E-3	0		0.031	0.667	--
HAP TOTAL						*1.200*	*4.566*									*12.564*				
MERCURY TOTAL (exempt)								*6.9E-4*	*2.8E-3*											
MERCURY TOTAL (non-exempt)										*1.3E-5*	*5.4E-5*						*5.4E-5*			
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)												*1.150*	*4.353*							
TAP TOTAL (For EL Evaluation)														*6.928*	*26.109*			*93.573*		

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 1 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

Model Scenario W3 T-RACT Emissions

Hazardous Air Pollutants (HAP)/Toxic Air Pollutants (TAP) Emissions Summary

		Emissions[1]									
		Fuel Combustion		Process/Prod/Leach		Mining		Total			
CAS	HAP/TAP	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	HAP	TAP
106-99-0	1,3-Butadiene	8.4E-07	3.7E-06	0	0	0	0	8.4E-07	3.7E-06	Y	Y
91-57-6	2-Methylnaphthalene	1.1E-06	4.6E-06	0	0	0	0	1.1E-06	4.6E-06	Y	N
56-49-5	3-Methylchloranthrene	7.8E-08	3.4E-07	0	0	0	0	7.8E-08	3.4E-07	Y	Y
57-97-6	7,12-Dimethylbenz(a)anthracene	7.6E-07	3.0E-06	0	0	0	0	7.6E-07	3.0E-06	Y	N
83-32-9	Acenaphthene	5.7E-06	7.1E-06	0	0	0	0	5.7E-06	7.1E-06	Y	N
208-96-8	Acenaphthylene	1.1E-05	1.4E-05	0	0	0	0	1.1E-05	1.4E-05	Y	N
75-07-0	Acetaldehyde	2.5E-05	1.1E-04	0	0	0	0	2.5E-05	1.1E-04	Y	Y
107-02-8	Acrolein	1.6E-05	2.0E-05	0	0	0	0	1.6E-05	2.0E-05	Y	Y
120-12-7	Anthracene	1.7E-06	2.4E-06	0	0	0	0	1.7E-06	2.4E-06	Y	N
7440-36-0	Antimony	0	0	5.7E-04	2.5E-03	1.3E-02	5.8E-02	1.4E-02	6.1E-02	Y	Y
7440-38-2	Arsenic	8.7E-06	3.8E-05	4.5E-03	2.0E-02	0.23	1.02	0.24	1.04	Y	Y
56-55-3	Benz(a)anthracene	3.1E-07	1.4E-06	0	0	0	0	3.1E-07	1.4E-06	Y	Y
71-43-2	Benzene	3.6E-04	1.6E-03	7.0E-03	3.1E-02	0	0	7.4E-03	3.2E-02	Y	Y
50-32-8	Benzo(a)pyrene	1.4E-07	6.1E-07	0	0	0	0	1.4E-07	6.1E-07	Y	Y
205-99-2	Benzo(b)fluoranthene	4.4E-07	1.9E-06	0	0	0	0	4.4E-07	1.9E-06	Y	Y
191-24-2	Benzo(g,h,i)perylene	7.5E-07	1.1E-06	0	0	0	0	7.5E-07	1.1E-06	Y	N
207-08-9	Benzo(k)fluoranthene	1.5E-07	6.6E-07	0	0	0	0	1.5E-07	6.6E-07	Y	Y
7440-41-7	Beryllium	5.2E-07	2.3E-06	4.3E-04	1.9E-03	1.9E-03	8.1E-03	2.3E-03	1.0E-02	Y	Y
92-52-4	Biphenyl	0	0	4.4E-05	1.9E-04	0	0	4.4E-05	1.9E-04	Y	Y
7440-43-9	Cadmium	4.8E-05	2.1E-04	4.1E-04	1.8E-03	2.9E-04	1.3E-03	7.5E-04	3.3E-03	Y	Y
75-15-0	Carbon Disulfide	0	0	1.4E-02	6.3E-02	0	0	1.4E-02	6.3E-02	Y	Y
7440-47-3	Chromium	6.6E-05	2.7E-04	6.1E-04	2.5E-03	5.2E-03	2.3E-02	5.9E-03	2.6E-02	Y	Y
18540-29-9	Cr (VI)	0	0	3.4E-07	1.5E-06	0	0	3.4E-07	1.5E-06	Y	Y
218-01-9	Chrysene	5.8E-07	2.5E-06	0	0	0	0	5.8E-07	2.5E-06	Y	Y
7440-48-4	Cobalt	4.0E-06	1.6E-05	4.7E-04	2.0E-03	2.3E-03	1.0E-02	2.8E-03	1.2E-02	Y	Y
592-01-8	Cyanide	0	0	0.45	1.99	0	0	0.45	1.99	Y	Y
53-70-3	Dibenzo(a,h)anthracene	1.8E-07	7.7E-07	0	0	0	0	1.8E-07	7.7E-07	Y	Y
106-46-7	Dichlorobenzene	5.7E-05	2.3E-04	0	0	0	0	5.7E-05	2.3E-04	Y	Y
206-44-0	Fluoranthene	5.5E-06	7.0E-06	0	0	0	0	5.5E-06	7.0E-06	Y	N
86-73-7	Fluorene	1.7E-05	2.1E-05	0	0	0	0	1.7E-05	2.1E-05	Y	N
50-00-0	Formaldehyde	3.3E-03	1.5E-02	0	0	0	0	3.3E-03	1.5E-02	Y	Y
110-54-3	Hexane	8.5E-02	0.34	3.1E-02	0.14	0	0	0.12	0.48	Y	Y
7647-01-0	Hydrogen Chloride	0	0	0.99	3.67	0	0	0.99	**3.67**	Y	Y
193-39-5	Indeno(1,2,3-cd)pyrene	2.2E-07	9.6E-07	0	0	0	0	2.2E-07	9.6E-07	Y	Y
7439-92-1	Lead	0	0	4.8E-04	2.1E-03	4.6E-03	2.0E-02	5.1E-03	2.2E-02	Y	N
7439-96-5	Manganese	1.8E-05	7.2E-05	4.6E-03	1.7E-02	0.17	0.76	0.18	0.78	Y	Y
7439-97-6	Mercury	1.2E-05	5.0E-05	6.9E-04	2.9E-03	1.2E-03	5.1E-03	1.9E-03	8.0E-03	Y	N
91-20-3	Naphthalene	1.9E-04	3.1E-04	1.9E-03	8.5E-03	0	0	2.1E-03	8.8E-03	Y	Y
7440-02-0	Nickel	9.1E-05	4.0E-04	4.6E-04	2.0E-03	1.2E-03	5.1E-03	1.7E-03	7.5E-03	Y	Y
85-01-8	Phenanthrene	5.1E-05	6.3E-05	0	0	0	0	5.1E-05	6.3E-05	Y	N
108-95-2	Phenol	0	0	2.4E-04	1.1E-03	0	0	2.4E-04	1.1E-03	Y	Y
7723-14-0	Phosphorus	0	0	5.6E-03	2.3E-02	0.38	1.65	0.38	1.67	Y	Y
129-00-0	Pyrene	5.0E-06	6.6E-06	0	0	0	0	5.0E-06	6.6E-06	Y	N
7782-49-2	Selenium	1.1E-06	4.6E-06	4.1E-04	1.8E-03	2.3E-04	1.0E-03	6.4E-04	2.8E-03	Y	Y
108-88-3	Toluene	5.2E-04	1.1E-03	3.2E-02	0.14	0	0	3.2E-02	0.14	Y	Y
1330-20-7	Xylene	2.5E-04	3.0E-04	3.1E-02	0.14	0	0	3.2E-02	0.14	Y	Y
Total HAP		9.0E-02	0.36	1.58	6.25	0.81	3.56	2.48	10.17		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

	0.2155	0.8650	8.3307	31.6474	61.0803	267.5316	69.6264	300.0439
TRUE	0.2155	0.8650	8.3307	31.6474	61.0803	267.5316	69.6264	300.0439
	chk	chk	chk-15	chk	chk	chk	chk-14	chk

Hazardous Air Pollutants (HAP)/Toxic Air Pollutants (TAP) Emissions Summary - continued

		Emissions[1]									
		Fuel Combustion		Process/Prod/Leach		Mining		Total			
CAS	**Non-HAP TAP**	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	HAP	TAP
7429-90-5	Aluminum	0	0	0.65	2.58	41.11	180.04	41.75	182.62	N	Y
7440-39-3	Barium	2.1E-04	8.4E-04	6.6E-03	2.7E-02	0.46	2.03	0.47	2.06	N	Y
1317-65-3	Calcium Carbonate	0	0	2.24	8.12	8.11	35.50	10.35	43.63	N	Y
1305-78-8	Calcium Oxide	0	0	0.70	0.95	0	0	0.70	0.95	N	Y
7440-50-8	Copper	4.0E-05	1.6E-04	4.9E-04	2.1E-03	2.9E-03	1.3E-02	3.4E-03	1.5E-02	N	Y
110-82-7	Cyclohexane	0	0	1.0E-03	4.6E-03	0	0	1.0E-03	4.6E-03	N	Y
7783-06-4	Hydrogen Sulfide	0	0	0.90	3.94	0	0	0.90	3.94	N	Y
7439-89-6	Iron	0	0	0.21	0.81	10.54	46.15	10.75	46.96	N	Y
7439-98-7	Molybdenum	5.2E-05	2.1E-04	4.2E-04	1.8E-03	5.8E-04	2.5E-03	1.0E-03	4.6E-03	N	Y
109-66-0	Pentane	0.12	0.50	0	0	0	0	0.12	0.50	N	Y
7440-22-4	Silver	0	0	4.1E-04	1.8E-03	2.9E-04	1.3E-03	7.0E-04	3.1E-03	N	Y
7664-93-9	Sulfuric Acid	0	0	2.03	8.89	0	0	2.03	8.89	N	Y
7440-28-0	Thallium	0	0	5.2E-04	2.2E-03	5.8E-03	2.5E-02	6.3E-03	2.8E-02	N	Y
7440-61-1	Uranium	0	0	5.2E-04	2.2E-03	5.8E-03	2.5E-02	6.3E-03	2.8E-02	N	Y
7440-62-2	Vanadium	1.1E-04	4.4E-04	7.3E-04	3.0E-03	1.6E-02	7.1E-02	1.7E-02	7.4E-02	N	Y
25551-13-7	Trimethyl benzene	0	0	1.1E-02	4.8E-02	0	0	1.1E-02	4.8E-02	N	Y
7440-33-7	Tungsten	0	0	5.2E-04	2.2E-03	5.8E-03	2.5E-02	6.3E-03	2.8E-02	N	Y
7440-66-6	Zinc	1.4E-03	5.5E-03	8.0E-04	3.3E-03	2.0E-02	8.9E-02	2.2E-02	9.8E-02	N	Y
Total Non-HAP TAP		0.13	0.50	6.75	25.40	60.27	263.98	67.15	289.88		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

Conversions

2,000 lb/ton
8,760 hr/yr
24 hr/day

PROPANE COMBUSTION

Source Data

Source ID	Description	MMBtu/day	MMBtu/yr
Lime Process Heating			
LKC	PFR Shaft Lime Kiln Combustion	529.0	163,935
Ore Process Heating			
ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	17.0	510
CKB	Carbon Regeneration Kiln (Burners)	54.1	19,754
PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	2.4	876
HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	120.0	43,800
Subtotal		193.5	64,940
HVAC			
H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	96.0	35,040
H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	96.0	35,040
HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	96.0	35,040
HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	12.0	4,380
HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	48.0	17,520
HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	72.0	26,280
Subtotal		438.0	159,870

PROPANE COMBUSTION - CONTINUED

HAP/TAP Emission Factors and Emissions

O.Heat_pph O.Heat_tpy L.Heat_pph L.Heat_tpy HVAC_pph HVAC_tpy lb/hr ton/yr

		Emission Factor[2]		Emissions[1] Ore Proc Heat		Lime Proc Heat		HVAC		Total			
CAS	Pollutant	lb/MMscf	lb/MMBtu[3]	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	TAP	A/C
91-57-6	2-Methylnaphthalene	2.4E-05	2.35E-8	1.9E-07	7.6E-07	5.2E-07	1.9E-06	4.3E-07	1.9E-06	1.1E-06	4.6E-06	N	
56-49-5	3-Methylchloranthrene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
57-97-6	7,12-Dimethylbenz(a)ant	< 1.6E-05	1.57E-8	1.3E-07	5.1E-07	3.5E-07	1.3E-06	2.9E-07	1.3E-06	7.6E-07	3.0E-06	N	
83-32-9	Acenaphthene	< 1.8E-06	1.76E-9	1.4E-08	5.7E-08	3.9E-08	1.4E-07	3.2E-08	1.4E-07	8.5E-08	3.4E-07	N	
208-96-8	Acenaphthylene	< 1.8E-06	1.76E-9	1.4E-08	5.7E-08	3.9E-08	1.4E-07	3.2E-08	1.4E-07	8.5E-08	3.4E-07	N	
120-12-7	Anthracene	< 2.4E-06	2.35E-9	1.9E-08	7.6E-08	5.2E-08	1.9E-07	4.3E-08	1.9E-07	1.1E-07	4.6E-07	N	
7440-38-2	Arsenic	2.0E-04	1.96E-7	1.5E-06	6.4E-06	3.7E-06	1.6E-05	3.6E-06	1.6E-05	8.7E-06	3.8E-05	Y	C
56-55-3	Benz(a)anthracene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
71-43-2	Benzene	2.1E-03	2.06E-6	1.5E-05	6.7E-05	3.9E-05	1.7E-04	3.8E-05	1.6E-04	9.1E-05	4.0E-04	Y	C
50-32-8	Benzo(a)pyrene	< 1.2E-06	1.18E-9	8.7E-09	3.8E-08	2.2E-08	9.6E-08	2.1E-08	9.4E-08	5.2E-08	2.3E-07	Y	C
205-99-2	Benzo(b)fluoranthene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
191-24-2	Benzo(g,h,i)perylene	< 1.2E-06	1.18E-9	9.5E-09	3.8E-08	2.6E-08	9.6E-08	2.1E-08	9.4E-08	5.7E-08	2.3E-07	N	
207-08-9	Benzo(k)fluoranthene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7440-41-7	Beryllium	< 1.2E-05	1.18E-8	8.7E-08	3.8E-07	2.2E-07	9.6E-07	2.1E-07	9.4E-07	5.2E-07	2.3E-06	Y	C
7440-43-9	Cadmium	1.1E-03	1.08E-6	8.0E-06	3.5E-05	2.0E-05	8.8E-05	2.0E-05	8.6E-05	4.8E-05	2.1E-04	Y	C
7440-47-3	Chromium	1.4E-03	1.37E-6	1.1E-05	4.5E-05	3.0E-05	1.1E-04	2.5E-05	1.1E-04	6.6E-05	2.7E-04	Y	A
218-01-9	Chrysene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7440-48-4	Cobalt	8.4E-05	8.24E-8	6.6E-07	2.7E-06	1.8E-06	6.8E-06	1.5E-06	6.6E-06	4.0E-06	1.6E-05	Y	A
53-70-3	Dibenzo(a,h)anthracene	< 1.2E-06	1.18E-9	8.7E-09	3.8E-08	2.2E-08	9.6E-08	2.1E-08	9.4E-08	5.2E-08	2.3E-07	Y	C
106-46-7	Dichlorobenzene	1.2E-03	1.18E-6	9.5E-06	3.8E-05	2.6E-05	9.6E-05	2.1E-05	9.4E-05	5.7E-05	2.3E-04	Y	A
206-44-0	Fluoranthene	3.0E-06	2.94E-9	2.4E-08	9.5E-08	6.5E-08	2.4E-07	5.4E-08	2.4E-07	1.4E-07	5.7E-07	N	
86-73-7	Fluorene	2.8E-06	2.75E-9	2.2E-08	8.9E-08	6.1E-08	2.3E-07	5.0E-08	2.2E-07	1.3E-07	5.3E-07	N	
50-00-0	Formaldehyde	7.5E-02	7.35E-5	5.5E-04	2.4E-03	1.4E-03	6.0E-03	1.3E-03	5.9E-03	3.3E-03	1.4E-02	Y	C
110-54-3	Hexane	1.8E+00	1.76E-3	1.4E-02	5.7E-02	3.9E-02	1.4E-01	3.2E-02	1.4E-01	8.5E-02	3.4E-01	Y	A
193-39-5	Indeno(1,2,3-cd)pyrene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7439-96-5	Manganese	3.8E-04	3.73E-7	3.0E-06	1.2E-05	8.2E-06	3.1E-05	6.8E-06	3.0E-05	1.8E-05	7.2E-05	Y	A
7439-97-6	Mercury	2.6E-04	2.55E-7	2.1E-06	8.3E-06	5.6E-06	2.1E-05	4.7E-06	2.0E-05	1.2E-05	5.0E-05	N	
91-20-3	Naphthalene	6.1E-04	5.98E-7	4.8E-06	1.9E-05	1.3E-05	4.9E-05	1.1E-05	4.8E-05	2.9E-05	1.2E-04	Y	A
7440-02-0	Nickel	2.1E-03	2.06E-6	1.5E-05	6.7E-05	3.9E-05	1.7E-04	3.8E-05	1.6E-04	9.1E-05	4.0E-04	Y	C
85-01-8	Phenanthrene	1.7E-05	1.67E-8	1.3E-07	5.4E-07	3.7E-07	1.4E-06	3.0E-07	1.3E-06	8.1E-07	3.2E-06	N	
129-00-0	Pyrene	5.0E-06	4.90E-9	4.0E-08	1.6E-07	1.1E-07	4.0E-07	8.9E-08	3.9E-07	2.4E-07	9.5E-07	N	
7782-49-2	Selenium	< 2.4E-05	2.35E-8	1.9E-07	7.6E-07	5.2E-07	1.9E-06	4.3E-07	1.9E-06	1.1E-06	4.6E-06	Y	A
108-88-3	Toluene	3.4E-03	3.33E-6	2.7E-05	1.1E-04	7.3E-05	2.7E-04	6.1E-05	2.7E-04	1.6E-04	6.5E-04	Y	A
109-66-0	Pentane	2.6E+00	2.55E-3	2.1E-02	8.3E-02	5.6E-02	2.1E-01	4.7E-02	2.0E-01	1.2E-01	5.0E-01	Y	A
7440-39-3	Barium	4.4E-03	4.31E-6	3.5E-05	1.4E-04	9.5E-05	3.5E-04	7.9E-05	3.4E-04	2.1E-04	8.4E-04	Y	A
7440-50-8	Copper	8.5E-04	8.33E-7	6.7E-06	2.7E-05	1.8E-05	6.8E-05	1.5E-05	6.7E-05	4.0E-05	1.6E-04	Y	A
7439-98-7	Molybdenum	1.1E-03	1.08E-6	8.7E-06	3.5E-05	2.4E-05	8.8E-05	2.0E-05	8.6E-05	5.2E-05	2.1E-04	Y	A
7440-62-2	Vanadium	2.3E-03	2.25E-6	1.8E-05	7.3E-05	5.0E-05	1.8E-04	4.1E-05	1.8E-04	1.1E-04	4.4E-04	Y	A
7440-66-6	Zinc	2.9E-02	2.84E-5	2.3E-04	9.2E-04	6.3E-04	2.3E-03	5.2E-04	2.3E-03	1.4E-03	5.5E-03	Y	A
Total				3.6E-02	1.4E-01	9.8E-02	3.6E-01	8.1E-02	3.5E-01	2.1E-01	8.6E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *AP-42, Table 1.4-3 & 1.4-4 (7/98) Natural Gas Combustion* 1.0766 1.0766

(3) *Natural Gas Higher Heating Value* 1,020 *MMBtu/MMscf* chk

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 5 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

DIESEL COMBUSTION

Source Data

Source ID	Description	Power Rating kW	Power Rating hp	Operation hr/day	Operation hr/yr	Fuel Consumption[1] & [2] MMBtu/day	Fuel Consumption[1] & [2] MMBtu/yr
EDG1	Camp Emergency Generator	1,000	1,341	1	100	9.39	938.70
EDG2	Plant Emergency Generator #1	1,000	1,341	1	100	9.39	938.7
EDG3	Plant Emergency Generator #2	1,000	1,341	1	100	9.39	938.7
EDFP	Mill Fire Pump	200	268	1	100	1.88	187.7
Total						30.0	3,003.8

(1) *Based on brake specific fuel consumption for diesel generators* 7,000 *Btu/hp-hr* *AP-42 Tbl 3.3-1*

(2) *Heat Content of* 0.137 *MMBtu/gal* 1E+6 *Btu/MMBtu* 1.341 *hp/kW*

HAP/TAP Emission Factors and Emissions

	Pollutant	Factor (lb/MMBtu) ≤600 hp[2]	Factor (lb/MMBtu) >600hp[3]	Emissions (≤600 hp) lb/hr	Emissions (≤600 hp) ton/yr	Emissions (>600 hp) lb/hr	Emissions (>600 hp) ton/yr	Total Emissions[1] lb/hr	Total Emissions[1] ton/yr	TAP	A/C
106-99-0	1,3-Butadiene	< 3.9E-05		8.4E-07	3.7E-06	0.0E+00	0.0E+00	8.4E-07	3.7E-06	Y	C
83-32-9	Acenaphthene	< 1.4E-06	4.7E-06	1.1E-07	1.3E-07	5.5E-06	6.6E-06	5.6E-06	6.7E-06	N	
208-96-8	Acenaphthylene	< 5.1E-06	9.2E-06	4.0E-07	4.7E-07	1.1E-05	1.3E-05	1.1E-05	1.3E-05	N	
75-07-0	Acetaldehyde	7.7E-04	2.5E-05	1.6E-05	7.2E-05	8.1E-06	3.5E-05	2.5E-05	1.1E-04	Y	C
107-02-8	Acrolein	< 9.3E-05	7.9E-06	7.2E-06	8.7E-06	9.2E-06	1.1E-05	1.6E-05	2.0E-05	Y	A
120-12-7	Anthracene	1.9E-06	1.2E-06	1.5E-07	1.8E-07	1.4E-06	1.7E-06	1.6E-06	1.9E-06	N	
56-55-3	Benz(a)anthracene	1.7E-06	6.2E-07	3.6E-08	1.6E-07	2.0E-07	8.8E-07	2.4E-07	1.0E-06	Y	C
71-43-2	Benzene	9.3E-04	7.8E-04	2.0E-05	8.8E-05	2.5E-04	1.1E-03	2.7E-04	1.2E-03	Y	C
50-32-8	Benzo(a)pyrene	< 1.9E-07	< 2.6E-07	4.0E-09	1.8E-08	8.3E-08	3.6E-07	8.7E-08	3.8E-07	Y	C
205-99-2	Benzo(b)fluoranthene	< 9.9E-08	< 1.1E-06	2.1E-09	9.3E-09	3.6E-07	1.6E-06	3.6E-07	1.6E-06	Y	C
191-24-2	Benzo(g,h,i)perylene	< 4.9E-07	< 5.6E-07	3.8E-08	4.6E-08	6.5E-07	7.8E-07	6.9E-07	8.3E-07	N	
207-08-9	Benzo(k)fluoranthene	< 1.6E-07	< 2.2E-07	3.3E-09	1.5E-08	7.0E-08	3.1E-07	7.3E-08	3.2E-07	Y	C
218-01-9	Chrysene	3.5E-07	1.5E-06	7.6E-09	3.3E-08	4.9E-07	2.2E-06	5.0E-07	2.2E-06	Y	C
53-70-3	Dibenzo(a,h)anthracene	< 5.8E-07	< 3.5E-07	1.2E-08	5.5E-08	1.1E-07	4.9E-07	1.2E-07	5.4E-07	Y	C
206-44-0	Fluoranthene	7.6E-06	4.0E-06	6.0E-07	7.1E-07	4.7E-06	5.7E-06	5.3E-06	6.4E-06	N	
86-73-7	Fluorene	2.9E-05	1.3E-05	2.3E-06	2.7E-06	1.5E-05	1.8E-05	1.7E-05	2.1E-05	N	
50-00-0	Formaldehyde	1.2E-03	7.9E-05	2.5E-05	1.1E-04	2.5E-05	1.1E-04	5.1E-05	2.2E-04	Y	C
193-39-5	Indeno(1,2,3-cd)pyrene	< 3.8E-07	< 4.1E-07	8.0E-09	3.5E-08	1.3E-07	5.8E-07	1.4E-07	6.2E-07	Y	C
91-20-3	Naphthalene	8.5E-05	1.3E-04	6.6E-06	8.0E-06	1.5E-04	1.8E-04	1.6E-04	1.9E-04	Y	A
85-01-8	Phenanthrene	2.9E-05	4.1E-05	2.3E-06	2.8E-06	4.8E-05	5.7E-05	5.0E-05	6.0E-05	N	
129-00-0	Pyrene	4.8E-06	3.7E-06	3.7E-07	4.5E-07	4.4E-06	5.2E-06	4.7E-06	5.7E-06	N	
108-88-3	Toluene	4.1E-04	2.8E-04	3.2E-05	3.8E-05	3.3E-04	4.0E-04	3.6E-04	4.3E-04	Y	A
1330-20-7	Xylene	2.9E-04	1.9E-04	2.2E-05	2.7E-05	2.3E-04	2.7E-04	2.5E-04	3.0E-04	Y	A
Total				1.4E-04	3.6E-04	1.1E-03	2.2E-03	1.2E-03	2.6E-03		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *AP-42, Tab. 3.3-2, 10/96, diesel engines (≤ 600 hp)*

(3) *AP-42, Tabs. 3.4-3 & 3.4-4, 10/96, large diesel engines (> 600 hp)*

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 6 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

ORE PROCESSING

Source Data

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
OC1	Loader Transfer of Ore to Grizzly	3.500	0.639
OC2	Grizzly to Apron Feeder	3.500	0.639
OC3	Apron Feeder to Dribble Conveyor	3.500	0.639
OC4	Apron Feeder to Vibrating Grizzly	3.500	0.639
OC5	Dribble Conveyor to Vibrating Grizzly	3.500	0.639
OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	3.500	0.639
OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	30.000	5.475
OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	3.500	0.639
OC9	Stockpile Transfers to Reclaim Conveyors	16.560	3.022
OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	16.560	3.022
OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	16.560	3.022
OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge C	33.120	6.044
OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	3.864	0.705
Total		141.164	25.762

HAP/TAP Emission Factors and Emissions

lb/hr ton/yr

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	667	3.9E-03	1.7E-02	Y	C
7440-41-7	Beryllium	3.2	1.9E-05	8.2E-05	Y	C
7440-43-9	Cadmium	0.50	2.9E-06	1.3E-05	Y	C
7440-48-4	Cobalt	4	2.4E-05	1.0E-04	Y	A
7440-47-3	Chromium	9	5.3E-05	2.3E-04	Y	A
7439-97-6	Mercury [3]	0.96	5.6E-06	2.5E-05	N	
7439-96-5	Manganese	299	1.8E-03	7.7E-03	Y	A
7440-02-0	Nickel	2	1.2E-05	5.2E-05	Y	C
7439-92-1	Lead	8	4.7E-05	2.1E-04	N	
7440-36-0	Antimony	23	1.4E-04	5.9E-04	Y	A
7723-14-0	Phosphorus	650	3.8E-03	1.7E-02	Y	A
7782-49-2	Selenium [4]	0.40	2.4E-06	1.0E-05	Y	A
7440-22-4	Silver	0.50	2.9E-06	1.3E-05	Y	A
7429-90-5	Aluminum	71,000	4.2E-01	1.8E+00	Y	A
7440-39-3	Barium	800	4.7E-03	2.1E-02	Y	A
1317-65-3	Calcium Carbonate	14,000	8.2E-02	3.6E-01	Y	A
7440-50-8	Copper	5	2.9E-05	1.3E-04	Y	A
7439-89-6	Iron [4]	18,200	1.1E-01	4.7E-01	Y	A
7439-98-7	Molybdenum	1	5.9E-06	2.6E-05	Y	A
7440-28-0	Thallium	10	5.9E-05	2.6E-04	Y	A
7440-61-1	Uranium	10	5.9E-05	2.6E-04	Y	A
7440-62-2	Vanadium	28	1.6E-04	7.2E-04	Y	A
7440-33-7	Tungsten	10	5.9E-05	2.6E-04	Y	A
7440-66-6	Zinc	35	2.1E-04	9.0E-04	Y	A
Total			6.2E-01	2.7E+00		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *(Midas Gold 2017c)* *Median concentration of 55,000 SGP samples.*

[3] *(Midas Gold 2018e)* *Median ore concentration of 151,000 SGP samples; resource block model.*

[4] *(Midas Gold 2020)* *Median concentration of 56,000 SGP samples for Fe and 1,500 SGP samples for Se.*

1E+6 parts/ppm

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 7 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

ORE CONCETRATION AND REFINING

Source Data

Source ID	Description	Subpart 7E Allowable Limit lb/yr[1]	Oper. hr/yr	% of Subpart 7E for Controlled Systems %	Controlled Hg Emissions lb/hr	ton/yr	lb/yr
AC	Autoclave	213.4	8,760	[2]	0.000023	0.00010	0.20
EW,MR,MF,CKD	Refinery Sources (C. Kiln, EW, Retort, Furn	16.8		20% [3]	0.000384	0.00168	3.36
7439-97-6 Mercury	Total	230.2			0.000407	0.00178	3.56

[1] *Subpart 7E Limit - Ore Pretreatment Processes (CFR 2018b)*

$$\frac{84\ lb}{MMton} \times \frac{2{,}540{,}400\ ton}{yr} \times \frac{MMton}{1.0E{+}6\ ton} = \frac{213.4\ lb}{yr}$$

[1] *Subpart 7E Limit - Carbon Processes with Mercury Retorts*

$$\frac{0.8\ lb}{ton} \times \frac{21\ ton}{yr} = \frac{16.8\ lb}{yr}$$

[2] *Controlled SysCAD modeled emissions from Autoclave:* 0.0105 g/hr 2.3E-05 lb/hr 0.20 lb/yr (M3 2019)

[3] *Based on similar source (but with much higher ore Hg content) Hg reporting levels provided below:*

Goldstrike Refinery (2015 & 2016 Hg Reports) (NDEP 2015a) (NDEP 2016)

$$\frac{28.79\ lb}{yr} \times \frac{yr}{251.00\ ton} = \frac{0.11\ lb}{MMton} \times \frac{ton}{0.8\ lb} = 14.3\%$$

Twin Creeks Refinery (2015 & 2016 Hg Reports) (NDEP 2015a) (NDEP 2016)

$$\frac{31.27\ lb}{yr} \times \frac{yr}{142.77\ ton} = \frac{0.22\ lb}{MMton} \times \frac{ton}{0.8\ lb} = 27.4\%$$

HAP/TAP Emission Factors and Emission

AC_pph AC_tpy Refin_pph Refin_tpy lb/hr ton/yr

CAS No.	Pollutant	Emission Factor[1]	Autoclave lb/hr	Autoclave ton/yr	Refinery lb/hr	Refinery ton/yr	Total Emissions lb/hr	Total Emissions ton/yr	TAP	A/C
7440-38-2	Arsenic	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-41-7	Beryllium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-43-9	Cadmium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-48-4	Cobalt	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-47-3	Chromium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-97-6	Mercury	see above	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	N	
7439-96-5	Manganese	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-02-0	Nickel	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7439-92-1	Lead	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	N	
7440-36-0	Antimony	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7723-14-0	Phosphorus	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7782-49-2	Selenium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-22-4	Silver	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7429-90-5	Aluminum	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-39-3	Barium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
1317-65-3	Calcium Carbonate	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-50-8	Copper	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-89-6	Iron	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-98-7	Molybdenum	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-28-0	Thallium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-61-1	Uranium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-62-2	Vanadium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-33-7	Tungsten	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-66-6	Zinc	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
Total			5.5E-04	2.4E-03	9.2E-03	4.0E-02	9.8E-03	4.3E-02		

[1] *Hg is the most difficult metal to control due to it existing in both particulate and gaseous form. Therefore, all other metals are conservatively estimated to be equal to or less than the Hg emissions.*

0.0525 0.0525 chk

7664-93-9	Sulfuric Acid	Autoclave	2.03	8.89			2.03	8.89
7783-06-4	Hydrogen Sulfid	Autoclave	0.90	3.94			0.90	3.94
592-01-8	Cyanide	Point Sources - 5 EW Cells			0.0012	0.0053	0.00	0.01
Total			2.93	12.84	0.01	0.05	2.94	12.88

ORE CONCETRATION AND REFINING - CONTINUED

Source Data

Source ID	Description	Throughput ton/day	Throughput ton/yr	Operation hr/day	Operation hr/yr
AC	Autoclave	6,960	2,540,400	24	8,760

Autoclave HAP/TAP Emission Factors and Emission lb/hr ton/yr

CAS No.	Pollutant	Emission Factor		Emissions[1] lb/hr	Emissions[1] ton/yr
7664-93-9	Sulfuric Acid	0.007	lb/ton[2]	2.03	8.89
7783-06-4	Hydrogen Sulfide	0.9	lb/hr[3]	0.90	3.94

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *H2SO4 is based on Acidic Autoclave test data (APT 2010)*

[3] *H2S is based on Acidic Autoclave test data (APT 2013)*

LEACHING OPERATION

Cyanide (HCN) Source Data, Emission Factors, and Emissions

Source ID	Description	Dia. ft[1]	pH[1]	Free CN- g/m3[1]	T C[1]	pKa	a0	H	kG[2] m/s	Fa*Fw	g/s	lb/hr	ton/yr
												lb/hr	ton/yr
TSF	***Fugitive Sources***												
TSF	Tailings Maint. Pond	76	7.75	1	3.74	9.803	0.9912	0.0025	1.89E-05	0.641	1.27E-05	0.0001	0.0004
MILLTA	CN Detox Tank 1	40	8.5	25	25	9.250	0.8490	0.0055	0.000311	0.688	0.002891	0.0229	0.101
MILLTA	CN Detox Tank 2	40	8.5	25	25	9.250	0.8490	0.0055	0.000311	0.688	0.002891	0.0229	0.101
MILLTA	CIP Leach Tank 1	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIP Leach Tank 2	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIP Leach Tank 3	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIP Leach Tank 4	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIL Tank 1	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 2	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 3	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 4	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 5	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 6	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIP Tank 1	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 2	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 3	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 4	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 5	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 6	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
		Acres[1]											
TSF	Tails, Aqueous Surface	110.222	7.75	1	3.74	9.803	0.9912	0.0025	1.89E-05	0.421	0.008845	0.0702	0.307
TSF	Tails, Wet Sediment	110.222							5.31E-08	0.421	0.009961	0.0791	0.346
TSF	Tails, Dry Sediment	110.222							2.33E-08	1	0.010375	0.0823	0.361
		330.666											
592-01-8	Cyanide Fugitive Sources - Subtotal											0.4527	1.983
75-15-0	Carbon Disulfide											0.01446	0.06332
	Point Sources												
EW	EW Cells	[3]										0.0006	0.003
EW	Preg/Barren Tanks	[3]										0.0006	0.003
592-01-8	Cyanide Point Sources - Subtotal											0.0012	0.0053
	Total											0.454	1.988

[1] *(Midas Gold 2016)(M3 2017c)(M3 2017d)*

[2] *The emission factors and caculation methodology are from the EPA directed HCN study: (Card, T. 2009)(EPA 2009)(Schmidt 2010)*

[3] *(APT 2009)*

Carbon Disulfide Emissions from Xanthate Decomposition

CAS No.	Pollutant	Xanthate[1] ton/yr	Molar Decomp.[2]	CS_2 MW Ratio	Temperature Adj. Factor[3]	Emissions lb/hr	Emissions ton/yr
						lb/hr	ton/yr
75-15-0	Carbon Disulfide	1,700	0.99%	0.376	1%	0.0145	0.063

	MW	
Xanthate (PAX)	202.37	$C6H11KOS_2$
Carbon disulfide	76.139	CS_2

[1] *(Midas Gold 2016) p. 12-11*

[2] *(Air Sciences 2020) molar decomposition of xanthate in solution to CS2 gas*

[3] *(Air Sciences 2020) based on the comparison of CS2 generation at 25C and 70C*

Conversions

8,760	hr/yr	453.5929	g/lb	Wind adjustment factor Fw	1
2,000	lb/ton	3.28084	ft/m		
4,046.86	m2/acre	3,600	s/hr		

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis		
	PROJECT NO: 335-20-3	PAGE: 10	OF: 19	SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021		

LIME PRODUCTION

Source Data

Source ID	Description	Throughput ton/day	Throughput ton/yr	PM Emissions lb/day	PM Emissions ton/yr
LS1	Limestone transfer to Primary Crusher Hopper			3.39	0.48
LS2	Primary Crushing and Associated Transfers In and Out			6.10	0.86
LS3	Primary Screening and Associated Transfers In and Out			28.25	3.97
LS4	Secondary Crushing and Associated Transfers In and Out			6.10	0.86
LS5	Secondary Screening and Associated Transfers In and Out			28.25	3.97
LS6	Limestone transfer to Ball Mill Feed Bin			3.39	0.48
LS7	Limestone transfer to Ball Mill Feed Conveyor			3.39	0.48
LS8	Ball Mill Feed transfer to Ball Mill			3.39	0.48
LSBM	Limestone Ball Mill			45.65	6.42
LS9	Limestone transfer to Kiln Feed Bin			0.80	0.12
LS10	Limestone transfer to Lime Kiln Feed Conveyor			0.80	0.12
LS11	Fines Screening and Associated Transfers In and Out			6.68	1.03
Subtotal LS1-11				136.18	19.28
LS12	Kiln Feed transfer to PFR Shaft Lime Kiln			0.80	0.12
LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	169	52,377	21.97	3.40
Subtotal LS12,LK				22.77	3.53
Total				158.95	22.80

HAP/TAP Emission Factors and Emissions

			LS_pph	LS_tpy	LS12_pph	LS12_tpy	LK_pph	LK_tpy	lb/hr	ton/yr		
		Concentration	LS1-11,LSBM		LS12		Lime Kiln		Emissions[1]			
CAS No.	Pollutant	ppm[2]	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.01E-04	4.43E-04	6.51E-07	2.85E-06	1.79E-05	7.83E-05	1.20E-04	5.24E-04	Y	C
7440-41-7	Beryllium	0.8	3.52E-06	1.54E-05	2.27E-08	9.92E-08	6.22E-07	2.72E-06	4.17E-06	1.82E-05	Y	C
7440-43-9	Cadmium	0.25	1.10E-06	4.82E-06	7.08E-09	3.10E-08	1.94E-07	8.51E-07	1.30E-06	5.70E-06	Y	C
7440-48-4	Cobalt	4	2.27E-05	7.71E-05	1.34E-07	4.96E-07	3.66E-06	1.36E-05	2.65E-05	9.12E-05	Y	A
7440-47-3	Chromium	15	8.51E-05	2.89E-04	5.01E-07	1.86E-06	1.37E-05	5.11E-05	9.93E-05	3.42E-04	Y	A
7439-97-6	Mercury [3]	0.02	1.13E-07	3.86E-07	6.68E-10	2.48E-09	2.82E-04	1.05E-03	2.82E-04	1.05E-03	N	
7439-96-5	Manganese	236.5	1.34E-03	4.56E-03	7.89E-06	2.93E-05	2.16E-04	8.05E-04	1.57E-03	5.39E-03	Y	A
7440-02-0	Nickel	5	2.20E-05	9.64E-05	1.42E-07	6.20E-07	3.89E-06	1.70E-05	2.60E-05	1.14E-04	Y	C
7439-92-1	Lead	3	1.70E-05	5.78E-05	1.00E-07	3.72E-07	2.75E-06	1.02E-05	1.99E-05	6.84E-05	N	
7440-36-0	Antimony	2.5	1.42E-05	4.82E-05	8.34E-08	3.10E-07	2.29E-06	8.51E-06	1.66E-05	5.70E-05	Y	A
7723-14-0	Phosphorus	130	7.38E-04	2.51E-03	4.34E-06	1.61E-05	1.19E-04	4.43E-04	8.61E-04	2.96E-03	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	1.28E-01	4.36E-01	7.54E-04	2.80E-03	2.07E-02	7.69E-02	1.50E-01	5.15E-01	Y	A
7440-39-3	Barium	145	8.23E-04	2.79E-03	4.84E-06	1.80E-05	1.33E-04	4.94E-04	9.60E-04	3.31E-03	Y	A
1317-65-3	Calcium Carbonate	274500	1.56E+00	5.29E+00	9.16E-03	3.40E-02	2.51E-01	9.35E-01	1.82E+00	6.26E+00	Y	A
7440-50-8	Copper	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7439-89-6	Iron	10350	5.87E-02	1.99E-01	3.45E-04	1.28E-03	9.47E-03	3.52E-02	6.85E-02	2.36E-01	Y	A
7439-98-7	Molybdenum	0.5	2.84E-06	9.64E-06	1.67E-08	6.20E-08	4.58E-07	1.70E-06	3.31E-06	1.14E-05	Y	A
7440-28-0	Thallium	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-61-1	Uranium	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-62-2	Vanadium	15.5	8.79E-05	2.99E-04	5.17E-07	1.92E-06	1.42E-05	5.28E-05	1.03E-04	3.53E-04	Y	A
7440-33-7	Tungsten	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-66-6	Zinc	18	1.02E-04	3.47E-04	6.01E-07	2.23E-06	1.65E-05	6.13E-05	1.19E-04	4.10E-04	Y	A
Subtotal			1.75E+00	5.94E+00	1.03E-02	3.82E-02	2.82E-01	1.05E+00	2.04E+00	7.03E+00	9.0667	9.0667
7647-01-0	Hydrogen Chloride	0.14 lb/ton product[4]					0.99	3.67	0.99	3.67		chk

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *(M3 2018) Median concentrations of SGP limestone material. Metals with medians below the detection limit (DL) are set to 1/2DL.*

[3] *Hg emissions from the Lime Kiln are conservatively estimated assuming 100% volatilization of all Hg in the limestone*

[4] *(EPA 1999b)*

1E+6 parts/ppm

LIME PRODUCTION - CONTINUED

Source Data

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
LS1L	Mill Lime Silo #1 Loading	0.248	0.002
LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	1.200	0.011
MillS2L	Mill Lime Silo #2 Loading	0.248	0.002
MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	1.200	0.011
ACS1L	AC Lime Silo #1 Loading	0.990	0.009
ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.304	0.042
ACS2L	AC Lime Silo #2 Loading	0.990	0.009
ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.304	0.042
ACS3L	AC Lime Silo #3 Loading	0.990	0.009
ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.304	0.042
ACS4L	AC Lime Silo #4 Loading	0.495	0.004
ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	2.304	0.021
Subtotal - Mill & AC Lime Silos		15.576	0.203
LCR	Lime Mill Crushing and associated transfers In and Out	6.828	1.058
LSL	Pebble Lime Silo Loading via Bucket Elevator	0.149	0.023
LSU	Pebble Lime Silo discharge to Lime Slaker	0.015	0.002
Subtotal - Lime Mfg		6.991	1.083
Total		22.567	1.286

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Mill and AC lb/hr	Mill and AC ton/yr	Lime Mfg lb/hr	Lime Mfg ton/yr	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.06E-06	4.66E-06	5.69E-06	2.49E-05	6.75E-06	2.96E-05	Y	C
7440-41-7	Beryllium	0.8	3.70E-08	1.62E-07	1.98E-07	8.67E-07	2.35E-07	1.03E-06	Y	C
7440-43-9	Cadmium	0.25	1.16E-08	5.07E-08	6.18E-08	2.71E-07	7.34E-08	3.22E-07	Y	C
7440-48-4	Cobalt	4	2.60E-06	8.11E-07	1.17E-06	4.33E-06	3.76E-06	5.14E-06	Y	A
7440-47-3	Chromium	15	9.74E-06	3.04E-06	4.37E-06	1.63E-05	1.41E-05	1.93E-05	Y	A
7439-97-6	Mercury	0.02	1.30E-08	4.05E-09	5.83E-09	2.17E-08	1.88E-08	2.57E-08	N	
7439-96-5	Manganese	236.5	1.53E-04	4.79E-05	6.89E-05	2.56E-04	2.22E-04	3.04E-04	Y	A
7440-02-0	Nickel	5	2.31E-07	1.01E-06	1.24E-06	5.42E-06	1.47E-06	6.43E-06	Y	C
7439-92-1	Lead	3	1.95E-06	6.08E-07	8.74E-07	3.25E-06	2.82E-06	3.86E-06	N	
7440-36-0	Antimony	2.5	1.62E-06	5.07E-07	7.28E-07	2.71E-06	2.35E-06	3.22E-06	Y	A
7723-14-0	Phosphorus	130	8.44E-05	2.63E-05	3.79E-05	1.41E-04	1.22E-04	1.67E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22,600	1.47E-02	4.58E-03	6.58E-03	2.45E-02	2.13E-02	2.91E-02	Y	A
7440-39-3	Barium	145	9.41E-05	2.94E-05	4.22E-05	1.57E-04	1.36E-04	1.86E-04	Y	A
1305-78-8	Calcium Oxide	740,000 [3]	4.80E-01	1.50E-01	2.16E-01	8.02E-01	6.96E-01	9.52E-01	Y	A
7440-50-8	Copper	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7439-89-6	Iron	10350	6.72E-03	2.10E-03	3.01E-03	1.12E-02	9.73E-03	1.33E-02	Y	A
7439-98-7	Molybdenum	0.5	3.25E-07	1.01E-07	1.46E-07	5.42E-07	4.70E-07	6.43E-07	Y	A
7440-28-0	Thallium	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-61-1	Uranium	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-62-2	Vanadium	15.5	1.01E-05	3.14E-06	4.52E-06	1.68E-05	1.46E-05	1.99E-05	Y	A
7440-33-7	Tungsten	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-66-6	Zinc	18	1.17E-05	3.65E-06	5.24E-06	1.95E-05	1.69E-05	2.31E-05	Y	A
Total			5.02E-01	1.57E-01	2.25E-01	8.38E-01	7.27E-01	9.95E-01		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *See LIME PRODUCTION, page 10*

[3] *(NLA 2007) 40% to 74% CaO in lime*

1E+6 parts/ppm

AGGREGATE PRODUCTION

Source Data

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conve	15.00	2.74
PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conve	15.00	2.74
Total		30.00	5.48

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	23	2.88E-05	1.26E-04	Y	C
7440-41-7	Beryllium	0.8	1.00E-06	4.38E-06	Y	C
7440-43-9	Cadmium	0.25	3.13E-07	1.37E-06	Y	C
7440-48-4	Cobalt	4	5.00E-06	2.19E-05	Y	A
7440-47-3	Chromium	15	1.88E-05	8.21E-05	Y	A
7439-97-6	Mercury	0.02	2.50E-08	1.10E-07	N	
7439-96-5	Manganese	236.5	2.96E-04	1.29E-03	Y	A
7440-02-0	Nickel	5	6.25E-06	2.74E-05	Y	C
7439-92-1	Lead	3	3.75E-06	1.64E-05	N	
7440-36-0	Antimony	2.5	3.13E-06	1.37E-05	Y	A
7723-14-0	Phosphorus	130	1.63E-04	7.12E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	2.83E-02	1.24E-01	Y	A
7440-39-3	Barium	145	1.81E-04	7.94E-04	Y	A
1317-65-3	Calcium Carbonate	274500	3.43E-01	1.50E+00	Y	A
7440-50-8	Copper	5	6.25E-06	2.74E-05	Y	A
7439-89-6	Iron	10350	1.29E-02	5.67E-02	Y	A
7439-98-7	Molybdenum	0.5	6.25E-07	2.74E-06	Y	A
7440-28-0	Thallium	5	6.25E-06	2.74E-05	Y	A
7440-61-1	Uranium	5	6.25E-06	2.74E-05	Y	A
7440-62-2	Vanadium	15.5	1.94E-05	8.49E-05	Y	A
7440-33-7	Tungsten	5	6.25E-06	2.74E-05	Y	A
7440-66-6	Zinc	18	2.25E-05	9.86E-05	Y	A
Total			3.85E-01	1.69E+00		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *See LIME PRODUCTION, page 10*

1E+6 parts/ppm

CONCRETE PRODUCTION

Source Data

Source ID	Description	Throughput ton/day	Throughput ton/yr
	description	TP_unit/day	TP_unit/yr
CS1L	Cement/Shotcrete Silo #1 Loading	164	60,000
CS1U	Cement/Shotcrete Silo #1 Unloading	164	60,000
CS2L	Cement/Shotcrete Silo #2 Loading	164	60,000
CS2U	Cement/Shotcrete Silo #2 Unloading	164	60,000
CM	Central Mixer Loading	164	60,000
	Subtotal Cement Silo Filling	658	240,000
	Subtotal Central Mix Batching	164	60,000

HAP/TAP Emission Factors and Emissions

CAS No.	HAP/TAP	Silo Fill lb/ton[2]	Central Mixer lb/ton[3]	Cement Silo L/U lb/hr (CF_pph)	Cement Silo L/U ton/yr (CF_tpy)	Central Mix Batching lb/hr (CM_pph)	Central Mix Batching ton/yr (CM_tpy)	Total Emissions[3] lb/hr	Total Emissions[3] ton/yr	TAP	A/C
7440-38-2	Arsenic	4.24E-09	2.96E-07	1.16E-7	5.09E-7	2.03E-6	8.88E-6	2.14E-6	9.39E-6	Y	C
7440-41-7	Beryllium	4.86E-10		1.33E-8	5.83E-8	--	--	1.33E-8	5.83E-8	Y	C
7440-43-9	Cadmium		7.10E-10	--	--	4.86E-9	2.13E-8	4.86E-9	2.13E-8	Y	C
7440-47-3	Chromium	2.90E-08	1.27E-07	7.95E-7	3.48E-6	8.70E-7	3.81E-6	1.66E-6	7.29E-6	Y	A
18540-29-9	Cr (VI)	5.80E-09	2.70E-08	1.59E-7	6.96E-7	1.85E-7	8.11E-7	3.44E-7	1.51E-6	Y	C
7439-92-1	Lead	1.09E-08	3.66E-08	2.99E-7	1.31E-6	2.51E-7	1.10E-6	5.49E-7	2.41E-6	N	
7439-96-5	Manganese	1.17E-07	3.78E-06	3.21E-6	1.40E-5	2.59E-5	1.13E-4	2.91E-5	1.27E-4	Y	A
7440-02-0	Nickel	4.18E-08	2.48E-07	1.15E-6	5.02E-6	1.70E-6	7.44E-6	2.84E-6	1.25E-5	Y	C
7723-14-0	Phosphorus		1.20E-06	--	--	8.22E-6	3.60E-5	8.22E-6	3.60E-5	Y	A
Total				5.73E-6	2.51E-5	3.91E-5	1.71E-4	4.49E-5	1.97E-4		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *AP-42, Table 11.12-8, (06/06) Cement Silo Filing, Controlled.* 20% *Cr (VI), IDEQ email on 11/23/2020* 0.0002 0.0002

(3) *AP-42, Table 11.12-8, (06/06) Central Mix Batching, Controlled.* 21.29% *Cr (VI), IDEQ email on 11/23/2020* chk

Conversions

24 hr/day

CONCRETE PRODUCTION - CONTINUED

Source Data

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
CAL	Aggregate Bin Loading	16.56	1.73
CAU	Aggregate Bin Unloading	16.56	1.73
Total		33.12	3.45

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.81E-05	7.94E-05	Y	C
7440-41-7	Beryllium	0.8	6.30E-07	2.76E-06	Y	C
7440-43-9	Cadmium	0.25	1.97E-07	8.63E-07	Y	C
7440-48-4	Cobalt	4	5.52E-06	1.38E-05	Y	A
7440-47-3	Chromium	15	2.07E-05	5.18E-05	Y	A
7439-97-6	Mercury	0.02	2.76E-08	6.90E-08	N	
7439-96-5	Manganese	236.5	3.26E-04	8.16E-04	Y	A
7440-02-0	Nickel	5	3.94E-06	1.73E-05	Y	C
7439-92-1	Lead	3	4.14E-06	1.04E-05	N	
7440-36-0	Antimony	2.5	3.45E-06	8.63E-06	Y	A
7723-14-0	Phosphorus	130	1.79E-04	4.49E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	3.12E-02	7.80E-02	Y	A
7440-39-3	Barium	145	2.00E-04	5.00E-04	Y	A
7440-50-8	Copper	5	6.90E-06	1.73E-05	Y	A
7439-89-6	Iron	10350	1.43E-02	3.57E-02	Y	A
7439-98-7	Molybdenum	0.5	6.90E-07	1.73E-06	Y	A
7440-28-0	Thallium	5	6.90E-06	1.73E-05	Y	A
7440-61-1	Uranium	5	6.90E-06	1.73E-05	Y	A
7440-62-2	Vanadium	15.5	2.14E-05	5.35E-05	Y	A
7440-33-7	Tungsten	5	6.90E-06	1.73E-05	Y	A
7440-66-6	Zinc	18	2.48E-05	6.21E-05	Y	A
Total			4.63E-02	1.16E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *See LIME PRODUCTION, page 10*

1E+6 parts/ppm

FUEL STORAGE - GASOLINE

Source Data

Source ID	description: Description	VOC_ppd: VOC Emissions lb/day	VOC_tpy: VOC Emissions ton/yr
TG1	Mine Site Gasoline Tank #1	5.25	0.96
TG2	Mine Site Gasoline Tank #2	5.25	0.96
Total		10.49	1.91

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration wt. %[2]	lb/hr: Emissions[1] lb/hr	ton/yr: Emissions[1] ton/yr	TAP	A/C
71-43-2	Benzene	1.608%	7.03E-03	3.08E-02	Y	C
92-52-4	Biphenyl	0.010%	4.37E-05	1.91E-04	Y	A
110-82-7	Cyclohexane	0.240%	1.05E-03	4.60E-03	Y	A
110-54-3	Hexane	7.138%	3.12E-02	1.37E-01	Y	A
91-20-3	Naphthalene	0.444%	1.94E-03	8.50E-03	Y	A
108-95-2	Phenol	0.055%	2.40E-04	1.05E-03	Y	A
108-88-3	Toluene	7.212%	3.15E-02	1.38E-01	Y	A
25551-13-7	Trimethyl benzene	2.500%	1.09E-02	4.79E-02	Y	A
1330-20-7	Xylene	7.170%	3.13E-02	1.37E-01	Y	A
Total			1.15E-01	5.05E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *(EPA 1999a)*

MINING FUGITIVE EMISSIONS

Dust Emissions

Source Data **Model Scenario** **W3** **T-RACT Emissions**

Operating schedule 365 day/yr

Clean rock cap (CR >50% [1]

[1] *(Perpetua 2021h) Percent of VMTs on haul roads capped with CR*

Roads outside of the pits and DRSFs are capped with CR

		PM Emissions	
Source ID	Description	lb/day	ton/yr
YPP	Yellow Pine Pit	--	--
HFP	Hangar Flats Pit	--	--
WEP	West End Pit	338.16	61.71
BT	Bradley Tailings	--	--
YPPBL	Yellow Pine Pit Blasting	--	--
HFPBL	Hangar Flats Pit Blasting	--	--
WEPBL	West End Pit Blasting	643.03	117.35
BTBL	Bradley Tailings Blasting	--	--
STKP	PC Stockpile	--	--
FDRSF	Fiddle DRSF	--	--
HFDRSF	Hangar Flats DRSF	152.12	27.76
YPDRSF	Yellow Pine DRSF	--	--
WEDRSF	West End DRSF	--	--
HR000	Haul Roads	12,723.41	2,322.02
TSF	Tailing Storage Facility	--	--
ACCRD	Access Roads	38.10	6.95
UGEXP	Scout Portal	0.008	0.002
Total		13,894.82	2,535.81

TSF, ACCRD, UGEXP 38.11 6.95 chk 2535.81

HAP/TAP Emission Factors		ORE	DR	CR	HRD	Borrow	AR
		Concentration					
CAS No.	Pollutant	ppm[1]	ppm[1]	ppm[3]	ppm[4]	ppm[5]	ppm
7440-38-2	Arsenic	667	667	90	378.5	2.5	2.5
7440-41-7	Beryllium	3.2	3.2		3.2		3.2
7440-43-9	Cadmium	0.5	0.5		0.5		0.5
7440-48-4	Cobalt	4	4		4		4
7440-47-3	Chromium	9	9		9		9
7439-97-6	Mercury [2]	0.96	0.6		0.6		0.6
7439-96-5	Manganese	299	299		299		299
7440-02-0	Nickel	2	2		2		2
7439-92-1	Lead	8	8		8		8
7440-36-0	Antimony	23	23		23		23
7723-14-0	Phosphorus	650	650		650		650
7782-49-2	Selenium	0.4	0.4		0.4		0.4
7440-22-4	Silver	0.5	0.5		0.5		0.5
7429-90-5	Aluminum	71000	71000		71000		71000
7440-39-3	Barium	800	800		800		800
1317-65-3	Calcium Carbonate	14000	14000		14000		14000
7440-50-8	Copper	5	5		5		5
7439-89-6	Iron	18200	18200		18200		18200
7439-98-7	Molybdenum	1	1		1		1
7440-28-0	Thallium	10	10		10		10
7440-61-1	Uranium	10	10		10		10
7440-62-2	Vanadium	28	28		28		28
7440-33-7	Tungsten	10	10		10		10
7440-66-6	Zinc	35	35		35		35

[1] *(Midas Gold 2017c)* *Median concentration of 55,000 SGP samples.* *1E+6 parts/ppm*

[2] *(Midas Gold 2018e)* *Median ore and development rock (DR) concentrations of 151,000 samples; resource block model.*

[3] *(Perpetua 2021g)* *Median concentration of 265 SGP samples.*

[4] *HRD: haul road - emissions calculated based on 50% of the total VMT occuring on CR*

[5] *(ALS 2018)* *Median concentration of 8 SGP samples.*

DR DR DR DR DR DR DR DR ORE DR DR DR DR HRD DR/AR

MINING FUGITIVE EMISSIONS - CONTINUED **Model Scenario W3** DR **T-RACT Emissions**

HAP/TAP Emissions

Hourly [1] YPP_pph HFP_pph WEP_pph BT_pph YPPBL_pph HFPBL_pph WEPBL_pph BTBL_pph STKP_pph FDRSF_pph HFDRSF_pph YPDRSF_pph WEDRSF_pph HR000_pph CCRD, UGE lb/hr

CAS No.	Pollutant	YPP lb/hr	HFP lb/hr	WEP lb/hr	BT lb/hr	YPPBL lb/hr	HFPBL lb/hr	WEPBL lb/hr	BTBL lb/hr	STKP lb/hr	FDRSF lb/hr	HFDRSF lb/hr	YPDRSF lb/hr	WEDRSF lb/hr	HR000 lb/hr	TSF, ACCRD, UGEXP lb/hr	Total lb/hr
7440-38-2	Arsenic	0	0	9.4E-3	0	0	0	0.018	0	0	0	4.2E-3	0	0	0.201	4.2E-6	0.232
7440-41-7	Beryllium	0	0	4.5E-5	0	0	0	8.6E-5	0	0	0	2.0E-5	0	0	1.7E-3	5.1E-6	1.9E-3
7440-43-9	Cadmium	0	0	7.0E-6	0	0	0	1.3E-5	0	0	0	3.2E-6	0	0	2.7E-4	7.9E-7	2.9E-4
7440-48-4	Cobalt	0	0	5.6E-5	0	0	0	1.1E-4	0	0	0	2.5E-5	0	0	2.1E-3	6.4E-6	2.3E-3
7440-47-3	Chromium	0	0	1.3E-4	0	0	0	2.4E-4	0	0	0	5.7E-5	0	0	4.8E-3	1.4E-5	5.2E-3
7439-97-6	Mercury	0	0	8.5E-6	0	0	0	1.6E-5	0	0	0	3.8E-6	0	0	3.2E-4	9.5E-7	3.5E-4
7439-96-5	Manganese	0	0	4.2E-3	0	0	0	8.0E-3	0	0	0	1.9E-3	0	0	0.159	4.7E-4	0.173
7440-02-0	Nickel	0	0	2.8E-5	0	0	0	5.4E-5	0	0	0	1.3E-5	0	0	1.1E-3	3.2E-6	1.2E-3
7439-92-1	Lead	0	0	1.1E-4	0	0	0	2.1E-4	0	0	0	5.1E-5	0	0	4.2E-3	1.3E-5	4.6E-3
7440-36-0	Antimony	0	0	3.2E-4	0	0	0	6.2E-4	0	0	0	1.5E-4	0	0	0.012	3.7E-5	0.013
7723-14-0	Phosphorus	0	0	9.2E-3	0	0	0	0.017	0	0	0	4.1E-3	0	0	0.345	1.0E-3	0.376
7782-49-2	Selenium	0	0	5.6E-6	0	0	0	1.1E-5	0	0	0	2.5E-6	0	0	2.1E-4	6.4E-7	2.3E-4
7440-22-4	Silver	0	0	7.0E-6	0	0	0	1.3E-5	0	0	0	3.2E-6	0	0	2.7E-4	7.9E-7	2.9E-4
7429-90-5	Aluminum	0	0	1.000	0	0	0	1.902	0	0	0	0.450	0	0	37.640	0.113	41.106
7440-39-3	Barium	0	0	0.011	0	0	0	0.021	0	0	0	5.1E-3	0	0	0.424	1.3E-3	0.463
1317-65-3	Calcium Ca	0	0	0.197	0	0	0	0.375	0	0	0	0.089	0	0	7.422	0.022	8.105
7440-50-8	Copper	0	0	7.0E-5	0	0	0	1.3E-4	0	0	0	3.2E-5	0	0	2.7E-3	7.9E-6	2.9E-3
7439-89-6	Iron	0	0	0.256	0	0	0	0.488	0	0	0	0.115	0	0	9.649	0.029	10.537
7439-98-7	Molybdenu	0	0	1.4E-5	0	0	0	2.7E-5	0	0	0	6.3E-6	0	0	5.3E-4	1.6E-6	5.8E-4
7440-28-0	Thallium	0	0	1.4E-4	0	0	0	2.7E-4	0	0	0	6.3E-5	0	0	5.3E-3	1.6E-5	5.8E-3
7440-61-1	Uranium	0	0	1.4E-4	0	0	0	2.7E-4	0	0	0	6.3E-5	0	0	5.3E-3	1.6E-5	5.8E-3
7440-62-2	Vanadium	0	0	3.9E-4	0	0	0	7.5E-4	0	0	0	1.8E-4	0	0	0.015	4.4E-5	0.016
7440-33-7	Tungsten	0	0	1.4E-4	0	0	0	2.7E-4	0	0	0	6.3E-5	0	0	5.3E-3	1.6E-5	5.8E-3
7440-66-6	Zinc	0	0	4.9E-4	0	0	0	9.4E-4	0	0	0	2.2E-4	0	0	0.019	5.6E-5	0.020
Total		0	0	1.490	0	0	0	2.834	0	0	0	0.670	0	0	55.918	0.167	61.079

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.* chk 61.0794 61.0794

DR DR DR DR DR DR DR DR ORE DR DR DR DR HRD DR/AR

MINING FUGITIVE EMISSIONS - CONTINUED **Model Scenario W3** DR **T-RACT Emissions**

HAP/TAP Emissions

Annual

		YPP_tpy	HFP_tpy	WEP_tpy	BT_tpy	YPPBL_tpy	HFPBL_tpy	WEPBL_tpy	BTBL_tpy	STKP_tpy	FDRSF_tpy	HFDRSF_tpy	YPDRSF_tpy	WEDRSF_tpy	HR000_tpy	CCRD, UGE	ton/yr
		YPP	HFP	WEP	BT	YPPBL	HFPBL	WEPBL	BTBL	STKP	FDRSF	HFDRSF	YPDRSF	WEDRSF	HR000	TSF, ACCRD, UGEXP	Total
CAS No.	Pollutant	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr
7440-38-2	Arsenic	0	0	0.041	0	0	0	0.078	0	0	0	0.019	0	0	0.879	1.8E-5	1.017
7440-41-7	Beryllium	0	0	2.0E-4	0	0	0	3.8E-4	0	0	0	8.9E-5	0	0	7.4E-3	2.2E-5	8.1E-3
7440-43-9	Cadmium	0	0	3.1E-5	0	0	0	5.9E-5	0	0	0	1.4E-5	0	0	1.2E-3	3.5E-6	1.3E-3
7440-48-4	Cobalt	0	0	2.5E-4	0	0	0	4.7E-4	0	0	0	1.1E-4	0	0	9.3E-3	2.8E-5	0.010
7440-47-3	Chromium	0	0	5.6E-4	0	0	0	1.1E-3	0	0	0	2.5E-4	0	0	0.021	6.3E-5	0.023
7439-97-6	Mercury	0	0	3.7E-5	0	0	0	7.0E-5	0	0	0	1.7E-5	0	0	1.4E-3	4.2E-6	1.5E-3
7439-96-5	Manganese	0	0	0.018	0	0	0	0.035	0	0	0	8.3E-3	0	0	0.694	2.1E-3	0.758
7440-02-0	Nickel	0	0	1.2E-4	0	0	0	2.3E-4	0	0	0	5.6E-5	0	0	4.6E-3	1.4E-5	5.1E-3
7439-92-1	Lead	0	0	4.9E-4	0	0	0	9.4E-4	0	0	0	2.2E-4	0	0	0.019	5.6E-5	0.020
7440-36-0	Antimony	0	0	1.4E-3	0	0	0	2.7E-3	0	0	0	6.4E-4	0	0	0.053	1.6E-4	0.058
7723-14-0	Phosphorus	0	0	0.040	0	0	0	0.076	0	0	0	0.018	0	0	1.509	4.5E-3	1.648
7782-49-2	Selenium	0	0	2.5E-5	0	0	0	4.7E-5	0	0	0	1.1E-5	0	0	9.3E-4	2.8E-6	1.0E-3
7440-22-4	Silver	0	0	3.1E-5	0	0	0	5.9E-5	0	0	0	1.4E-5	0	0	1.2E-3	3.5E-6	1.3E-3
7429-90-5	Aluminum	0	0	4.382	0	0	0	8.332	0	0	0	1.971	0	0	165	0.494	180
7440-39-3	Barium	0	0	0.049	0	0	0	0.094	0	0	0	0.022	0	0	1.858	5.6E-3	2.029
1317-65-3	Calcium Ca	0	0	0.864	0	0	0	1.643	0	0	0	0.389	0	0	32.508	0.097	35.501
7440-50-8	Copper	0	0	3.1E-4	0	0	0	5.9E-4	0	0	0	1.4E-4	0	0	0.012	3.5E-5	0.013
7439-89-6	Iron	0	0	1.123	0	0	0	2.136	0	0	0	0.505	0	0	42.261	0.127	46.152
7439-98-7	Molybdenu	0	0	6.2E-5	0	0	0	1.2E-4	0	0	0	2.8E-5	0	0	2.3E-3	7.0E-6	2.5E-3
7440-28-0	Thallium	0	0	6.2E-4	0	0	0	1.2E-3	0	0	0	2.8E-4	0	0	0.023	7.0E-5	0.025
7440-61-1	Uranium	0	0	6.2E-4	0	0	0	1.2E-3	0	0	0	2.8E-4	0	0	0.023	7.0E-5	0.025
7440-62-2	Vanadium	0	0	1.7E-3	0	0	0	3.3E-3	0	0	0	7.8E-4	0	0	0.065	1.9E-4	0.071
7440-33-7	Tungsten	0	0	6.2E-4	0	0	0	1.2E-3	0	0	0	2.8E-4	0	0	0.023	7.0E-5	0.025
7440-66-6	Zinc	0	0	2.2E-3	0	0	0	4.1E-3	0	0	0	9.7E-4	0	0	0.081	2.4E-4	0.089
Total		0	0	6.527	0	0	0	12.412	0	0	0	2.936	0	0	245	0.731	268
															chk	267.5280	267.5280

MINING FUGITIVE EMISSIONS - CONTINUED

Mercury Evaporative Flux Emissions

Fugitive Mercury Flux and Emissions

			Area		Hg Flux	Emissions[1] lb/hr	ton/yr	lb/yr
CAS No.	Pollutant	Source	m^2	ha	µg/m^2-yr	lb/hr	ton/yr	lb/yr
		Stockpiles	52,623	5.3	556	7.37E-6	3.2E-5	6.5E-2
		Rock Dumps	2,063,990	206.4	76.2	3.96E-5	1.7E-4	0.35
		Tailings	1,338,158	133.8	2,144	7.22E-4	3.2E-3	6.32
		Pits	1,504,919	150.5	132.3	5.01E-5	2.2E-4	0.44
7439-97-6	Mercury					8.2E-4	3.6E-3	7.17

(1) *Hourly emissions based on:* 8,760 *hours per year of operation*

Fugitive Mercury Emission Factors

	Twin Creeks (TC)		Ore Hg Adjusted	Stibnite	
	Hg Flux (1)	Hg (2)	µg/m^2/yr	Hg Flux (3)	Hg (4)
Source	µg/m^2-yr	µg/g	TC	µg/m^2-yr	µg/g
Stockpiles	5,609	33	556	556	0.96
Rock Dumps	768	3.5	76.2	76.2	0.60
Tailings	21,621	33	2,144	2,144	0.96
Pits	1,334	9.5	132	132.3	0.60

(1) *(Eckley 2010)* *Table 1: Hg flux µg/m^2-yr*

(2) *(Eckley 2010)* *Table 1: Average Hg flux mg/g: " Stockpiles - high-grade stockpiles, Rock Dumps - waste rock dumps, Tailings - high-grade stockpiles as a surrogate; Pits - pit"*

(3) *(Eckley 2010)* *Figure 2: log(y) = m*log(x) + b*

y = Hg Flux (ng/m^2-d)
x = material Hg concentration (µg/g)]

Slope =	*Solar*	*TC*
	Low	*0.59*
	Medium	*0.6*
	High	*0.77*
	Average	*0.65*

(4) *(Midas Gold 2018e)*

Sample Calculation: m = log (y1/y2) / log(x1/x2)

m=	0.65	unitless
y1=	5,609	µg/m^2-yr
x1=	33	µg/m^2-yr
x2=	0.96	µg/m^2-yr
log(x1/x2)=	1.536243	unitless
log(y1/y2)=	1.003679	unitless
y1/y2=	10.08506	unitless
y2=	556.2	µg/m^2-yr

Conversions

2,000	lb/ton
10,000	m2/ha
453.593	g/lb

TABLE A-W3. HAP/TAP Emissions and Exemptions

T-RACT Emissions						MINING										LEACHING	
chk						*Mining*		*Model Scenario*	*W3*							*CN Leach/PAX*	
						YPP,HFP,WEP,BT		YPPBL,HFPBL,WEPBL,BTBL		HR000		STKP, FDRSF, HFDRSF, YPDRSF, WEDRSF		TSF,ACCRD,UGEXP			
CAS	HAP/TAP	HAP	TAP			Pits		Blasting		Haul Roads		Stockpiles and DRFS		Tails, Access Road, Exploration		CN Leach and PAX	
	NSPS or NESHAP HAP/TAP -->			*Y*													
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				A/C	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
7440-38-2	Arsenic	Y	Y	Y	C	9.4E-3	0.041	0.018	0.078	0.201	0.879	4.2E-3	0.019	4.2E-6	1.8E-5		
7440-41-7	Beryllium	Y	Y	Y	C	4.5E-5	2.0E-4	8.6E-5	3.8E-4	1.7E-3	7.4E-3	2.0E-5	8.9E-5	5.1E-6	2.2E-5		
7440-43-9	Cadmium	Y	Y	Y	C	7.0E-6	3.1E-5	1.3E-5	5.9E-5	2.7E-4	1.2E-3	3.2E-6	1.4E-5	7.9E-7	3.5E-6		
50-00-0	Formaldehyde	Y	Y	Y	C												
7440-02-0	Nickel	Y	Y	Y	C	2.8E-5	1.2E-4	5.4E-5	2.3E-4	1.1E-3	4.6E-3	1.3E-5	5.6E-5	3.2E-6	1.4E-5		

TABLE A-W3. HAP/TAP Emissions and Exemptions

T-RACT Emissions						PROCESSING AND PRODUCTION											
chk						*Ore Processing*				*Ore Concentration and Refining*				*Process Heating*			
						OC1-13		PS		AC		EW,MR,MF,CKD		ACB, CKB, PV, HS		LKC	
CAS	HAP/TAP	HAP	TAP			Crushers & Xfers		Prill Silos		Autoclave		EW, Preg Tank, Retort, Furnace, Carbon Kiln		POX Boiler, C. Kiln Comb., Prop. Vap., Sol'n Heater		Lime Kiln Combustion	
	NSPS or NESHAP HAP/TAP -->			*Y*		***LL***	***LL***			***7E***	***7E***	***7E***	***7E***			***5A***	***5A***
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				**A/C**	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
7440-38-2	Arsenic	Y	Y	Y	C	3.9E-3	0.017			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.5E-6	6.4E-6	3.7E-6	1.6E-5
7440-41-7	Beryllium	Y	Y	Y	C	1.9E-5	8.2E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.7E-8	3.8E-7	2.2E-7	9.6E-7
7440-43-9	Cadmium	Y	Y	Y	C	2.9E-6	1.3E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.0E-6	3.5E-5	2.0E-5	8.8E-5
50-00-0	Formaldehyde	Y	Y	Y	C									5.5E-4	2.4E-3	1.4E-3	6.0E-3
7440-02-0	Nickel	Y	Y	Y	C	1.2E-5	5.2E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.5E-5	6.7E-5	3.9E-5	1.7E-4

TABLE A-W3. HAP/TAP Emissions and Exemptions

T-RACT Emissions						PROCESSING AND PRODUCTION - Continued													
chk						*Lime Production*						*Aggregate Prod.*		*Concrete Production*					
						LS1-11,LSBM		LK,LS12,LCR,LS-L/U		LS1-L/U,MillS2-L/U,ACS1-4		PCSP1,PCSP2		CM		CS1L,CS1U,CS2L, CS2U		CA-L/U	
CAS	HAP/TAP	HAP	TAP			Limestone Crushers, Screens, Mill, Xfers		Lime Kiln, Kiln Feed, Lime Mill, Pebble Lime Silo		Lime Silos and Lime Mill Crushing		Portable Crushers, Screens, Xfers		Central Mixer		Cement Silo #1 and #2 L/U		Aggregate Bin	
	NSPS or NESHAP HAP/TAP -->			*Y*		*OOO*	*OOO*	*5A*	*5A*			*OOO*	*OOO*					*OOO*	*OOO*
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
7440-38-2	Arsenic	Y	Y	Y	C	1.0E-4	4.4E-4	2.4E-5	1.1E-4	1.1E-6	4.7E-6	2.9E-5	1.3E-4	2.0E-6	8.9E-6	1.2E-7	5.1E-7	1.8E-5	7.9E-5
7440-41-7	Beryllium	Y	Y	Y	C	3.5E-6	1.5E-5	8.4E-7	3.7E-6	3.7E-8	1.6E-7	1.0E-6	4.4E-6			1.3E-8	5.8E-8	6.3E-7	2.8E-6
7440-43-9	Cadmium	Y	Y	Y	C	1.1E-6	4.8E-6	2.6E-7	1.2E-6	1.2E-8	5.1E-8	3.1E-7	1.4E-6	4.9E-9	2.1E-8			2.0E-7	8.6E-7
50-00-0	Formaldehyde	Y	Y	Y	C														
7440-02-0	Nickel	Y	Y	Y	C	2.2E-5	9.6E-5	5.3E-6	2.3E-5	2.3E-7	1.0E-6	6.3E-6	2.7E-5	1.7E-6	7.4E-6	1.1E-6	5.0E-6	3.9E-6	1.7E-5

TABLE A-W3. HAP/TAP Emissions and Exemptions

T-RACT Emissions						PROCESSING AND PRODUCTION - Continued						MINING and LEACHING - Totals									
chk						*HVAC*		*Emer. Power/Fire*		*Fuel Storage*		*HAP Total*		*Mercury Total*		*Mercury Total*		*TAP Total*		*TAP Total*	
						H1M,H2M,HM,HAC,HR,HA,HMO,HTS,HW		EDG1,EDG2,EDG3,EDFP		TG1,TG2				*Exempt*		*Non-Exempt*		*HAP-TAP addressed by NSPS/NESHAP*		*For EL Evaluation*	
CAS	HAP/TAP	HAP	TAP			Heaters		Emergency Generators and Fire Pump		Gasoline Fuel Tanks											
	NSPS or NESHAP HAP/TAP -->			*Y*				*4Z*	*4Z*	*6C*	*6C*										
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
7440-38-2	Arsenic	Y	Y	Y	C	3.6E-6	1.6E-5					0.232	1.017							0.232	1.017
7440-41-7	Beryllium	Y	Y	Y	C	2.1E-7	9.4E-7					1.9E-3	8.1E-3							1.9E-3	8.1E-3
7440-43-9	Cadmium	Y	Y	Y	C	2.0E-5	8.6E-5					2.9E-4	1.3E-3							2.9E-4	1.3E-3
50-00-0	Formaldehyde	Y	Y	Y	C	1.3E-3	5.9E-3	5.1E-5	2.2E-4												
7440-02-0	Nickel	Y	Y	Y	C	3.8E-5	1.6E-4					1.2E-3	5.1E-3					0	0	1.2E-3	5.1E-3

TABLE A-W3. HAP/TAP Emissions and Exemptions

T-RACT Emissions						PROCESSING AND PRODUCTION - Totals										ALL	ALL	ALL	TAP EL	
chk						*HAP Total*		*Mercury Total Exempt*		*Mercury Total Non-Exempt*		*TAP Total HAP-TAP addressed by NSPS/NESHAP*		*TAP Total For EL Evaluation*		*HAP*	*Hg Non-Exempt*	*TAP For EL Evaluation*	*TAP Emission Screening Level (EL)*	
CAS	HAP/TAP	HAP	TAP																	
	NSPS or NESHAP HAP/TAP -->	*Y*																	Non-car	Carcin
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	ton/yr	ton/yr	lb/hr	lb/hr	lb/hr
7440-38-2	Arsenic	Y	Y	Y	C	4.5E-3	0.020					4.5E-3	0.020	8.2E-6	3.6E-5	1.037		0.232	--	1.5E-6
7440-41-7	Beryllium	Y	Y	Y	C	4.3E-4	1.9E-3					4.3E-4	1.9E-3	3.5E-7	1.5E-6	0.010		1.9E-3	--	2.8E-5
7440-43-9	Cadmium	Y	Y	Y	C	4.6E-4	2.0E-3					4.3E-4	1.9E-3	2.8E-5	1.2E-4	3.3E-3		3.2E-4	--	3.7E-6
50-00-0	Formaldehyde	Y	Y	Y	C	3.3E-3	0.015					1.4E-3	6.2E-3	1.9E-3	8.3E-3	0.015		1.9E-3	--	5.1E-4
7440-02-0	Nickel	Y	Y	Y	C	5.5E-4	2.4E-3					4.9E-4	2.2E-3	5.6E-5	2.4E-4	7.5E-3		1.2E-3	--	2.7E-5

Appendix B – Modeled Emissions per Modeling Scenario and Source

Appendix B Table of Contents

Non-Carcinogenic TAP Modeling

Carcinogenic TAP Modeling

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: Y1	YPP	Yellow Pine Pit	0	0.024	0.051	5.585	0.063	1.101
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	4.5E-3	9.7E-3	1.063	0.012	0.210
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.065	0.141	15.394	0.173	3.035
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.102**	**0.220**	**24.705**	**0.278**	**6.987**

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: Y1	YPP	Yellow Pine Pit	0	1.432	0	7.9E-4	2.2E-3
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0.272	0	1.5E-4	4.2E-4
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	3.946	0	2.2E-3	6.1E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**6.380**	**2.030**	**3.9E-3**	**0.010**

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: Y2	YPP	Yellow Pine Pit	0	0.024	0.051	5.585	0.063	1.101
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.096	0.208	22.711	0.256	4.478
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.131**	**0.285**	**31.817**	**0.358**	**8.390**

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: Y2	YPP	Yellow Pine Pit	0	1.432	0	7.9E-4	2.2E-3
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0.220	0	1.2E-4	3.4E-4
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	5.822	0	3.2E-3	9.0E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.203**	**2.030**	**4.9E-3**	**0.013**

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: Y3	YPP	Yellow Pine Pit	0	0.024	0.051	5.585	0.063	1.101
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.155	0.337	36.835	0.415	7.263
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.191**	**0.415**	**45.941**	**0.517**	**11.175**

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: Y3	YPP	Yellow Pine Pit	0	1.432	0	7.9E-4	2.2E-3
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0.220	0	1.2E-4	3.4E-4
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	9.442	0	5.2E-3	0.015
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**11.823**	**2.030**	**6.9E-3**	**0.019**

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: H1	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0.024	0.051	5.585	0.063	1.101
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	4.5E-3	9.7E-3	1.063	0.012	0.210
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.105	0.228	24.940	0.281	4.918
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.142**	**0.308**	**34.252**	**0.385**	**8.870**

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: H1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	1.432	0	7.9E-4	2.2E-3
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0.272	0	1.5E-4	4.2E-4
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	6.393	0	3.5E-3	9.8E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.827**	**2.030**	**5.2E-3**	**0.014**

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: H2	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0.024	0.051	5.585	0.063	1.101
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.157	0.342	37.334	0.421	7.362
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.193**	**0.419**	**46.440**	**0.523**	**11.273**

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: H2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	1.432	0	7.9E-4	2.2E-3
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0.220	0	1.2E-4	3.4E-4
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	9.570	0	5.3E-3	0.015
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**11.951**	**2.030**	**7.0E-3**	**0.019**

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: H3	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0.024	0.051	5.585	0.063	1.101
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.096	0.209	22.854	0.258	4.506
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.132**	**0.287**	**31.960**	**0.360**	**8.418**

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: H3	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	1.432	0	7.9E-4	2.2E-3
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0.220	0	1.2E-4	3.4E-4
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	5.858	0	3.2E-3	9.0E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.239**	**2.030**	**4.9E-3**	**0.013**

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8 (24-hr) lb/hr	Manganese 7439-96-5 (24-hr) lb/hr	Phosphorus 7723-14-0 (24-hr) lb/hr	Aluminum 7429-90-5 (24-hr) lb/hr	Barium 7440-39-3 (24-hr) lb/hr	Calcium Carbonate 1317-65-3 (24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: H4	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0.024	0.051	5.585	0.063	1.101
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.123	0.268	29.277	0.330	5.773
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.159**	**0.346**	**38.383**	**0.432**	**9.685**

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: H4	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	1.432	0	7.9E-4	2.2E-3
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0.220	0	1.2E-4	3.4E-4
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	7.505	0	4.1E-3	0.012
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**9.886**	**2.030**	**5.8E-3**	**0.016**

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8 (24-hr) lb/hr	Manganese 7439-96-5 (24-hr) lb/hr	Phosphorus 7723-14-0 (24-hr) lb/hr	Aluminum 7429-90-5 (24-hr) lb/hr	Barium 7440-39-3 (24-hr) lb/hr	Calcium Carbonate 1317-65-3 (24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W1	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	4.5E-3	9.7E-3	1.063	0.012	0.210
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.090	0.196	21.435	0.242	4.227
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.127**	**0.276**	**30.746**	**0.346**	**8.179**

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0.272	0	1.5E-4	4.2E-4
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	5.495	0	3.0E-3	8.5E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**7.928**	**2.030**	**4.8E-3**	**0.013**

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8 (24-hr) lb/hr	Manganese 7439-96-5 (24-hr) lb/hr	Phosphorus 7723-14-0 (24-hr) lb/hr	Aluminum 7429-90-5 (24-hr) lb/hr	Barium 7440-39-3 (24-hr) lb/hr	Calcium Carbonate 1317-65-3 (24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W2	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.145	0.316	34.484	0.389	6.800
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.181**	**0.393**	**43.590**	**0.491**	**10.711**

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0.220	0	1.2E-4	3.4E-4
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	8.840	0	4.9E-3	0.014
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**11.221**	**2.030**	**6.6E-3**	**0.018**

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8 (24-hr) lb/hr	Manganese 7439-96-5 (24-hr) lb/hr	Phosphorus 7723-14-0 (24-hr) lb/hr	Aluminum 7429-90-5 (24-hr) lb/hr	Barium 7440-39-3 (24-hr) lb/hr	Calcium Carbonate 1317-65-3 (24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W3	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.208	0.452	49.397	0.557	9.740
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.244**	**0.530**	**58.504**	**0.659**	**13.652**

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W3	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0.220	0	1.2E-4	3.4E-4
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	12.662	0	7.0E-3	0.019
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**15.043**	**2.030**	**8.7E-3**	**0.024**

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W4	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.094	0.204	22.281	0.251	4.393
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.130**	**0.282**	**31.387**	**0.353**	**8.305**

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W4	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0.220	0	1.2E-4	3.4E-4
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	5.711	0	3.1E-3	8.8E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.092**	**2.030**	**4.8E-3**	**0.013**

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W5	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	HR000	Haul Roads	0	0.104	0.225	24.595	0.277	4.850
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.139**	**0.303**	**33.702**	**0.379**	**8.761**

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W5	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0.220	0	1.2E-4	3.4E-4
	HR000	Haul Roads	0	6.305	0	3.5E-3	9.7E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.686**	**2.030**	**5.2E-3**	**0.014**

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: B1	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0.023	0.051	5.567	0.063	1.098
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	STKP	PC Stockpile	0	4.5E-3	9.7E-3	1.063	0.012	0.210
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.120	0.260	28.394	0.320	5.599
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.156**	**0.339**	**37.687**	**0.424**	**9.547**

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: B1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	1.427	0	7.8E-4	2.2E-3
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0.488	0	2.7E-4	7.5E-4
	STKP	PC Stockpile	0	0.272	0	1.5E-4	4.2E-4
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	7.278	0	4.0E-3	0.011
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**9.707**	**2.030**	**5.7E-3**	**0.015**

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8 (24-hr) lb/hr	Manganese 7439-96-5 (24-hr) lb/hr	Phosphorus 7723-14-0 (24-hr) lb/hr	Aluminum 7429-90-5 (24-hr) lb/hr	Barium 7440-39-3 (24-hr) lb/hr	Calcium Carbonate 1317-65-3 (24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: B2	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0.023	0.051	5.567	0.063	1.098
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.028	0.061	6.713	0.076	1.324
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.064**	**0.139**	**15.801**	**0.178**	**5.232**

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: B2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	1.427	0	7.8E-4	2.2E-3
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0.488	0	2.7E-4	7.5E-4
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0.220	0	1.2E-4	3.4E-4
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	1.721	0	9.5E-4	2.6E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**4.097**	**2.030**	**2.7E-3**	**6.8E-3**

TABLE B-Y1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-Y1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-Y1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: Y1	YPP	Yellow Pine Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	5.7E-3	2.7E-5	4.3E-6	0	1.7E-5
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.065	5.5E-4	8.5E-5	0	3.4E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.098**	**7.1E-4**	**1.4E-4**	**1.9E-3**	**5.0E-4**

TABLE B-Y2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-Y2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-Y2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: Y2	YPP	Yellow Pine Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.094	7.9E-4	1.2E-4	0	5.0E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.125**	**9.5E-4**	**1.8E-4**	**1.9E-3**	**6.5E-4**

TABLE B-Y3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-Y3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-Y3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: Y3	YPP	Yellow Pine Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.150	1.3E-3	2.0E-4	0	7.9E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.182**	**1.4E-3**	**2.5E-4**	**1.9E-3**	**9.5E-4**

TABLE B-H1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-H1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-H1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: H1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	5.7E-3	2.7E-5	4.3E-6	0	1.7E-5
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.103	8.7E-4	1.4E-4	0	5.4E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.136**	**1.0E-3**	**1.9E-4**	**1.9E-3**	**7.0E-4**

TABLE B-H2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-H2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-H2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: H2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.152	1.3E-3	2.0E-4	0	8.1E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.184**	**1.4E-3**	**2.5E-4**	**1.9E-3**	**9.6E-4**

TABLE B-H3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-H3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-H3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: H3	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.095	8.0E-4	1.2E-4	0	5.0E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.126**	**9.6E-4**	**1.8E-4**	**1.9E-3**	**6.5E-4**

TABLE B-H4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-H4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-H4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: H4	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.120	1.0E-3	1.6E-4	0	6.4E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.152**	**1.2E-3**	**2.1E-4**	**1.9E-3**	**7.9E-4**

TABLE B-W1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	5.7E-3	2.7E-5	4.3E-6	0	1.7E-5
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.089	7.5E-4	1.2E-4	0	4.7E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.122**	**9.1E-4**	**1.7E-4**	**1.9E-3**	**6.3E-4**

TABLE B-W2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.141	1.2E-3	1.9E-4	0	7.5E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.173**	**1.3E-3**	**2.4E-4**	**1.9E-3**	**9.0E-4**

TABLE B-W3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W3	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.201	1.7E-3	2.7E-4	0	1.1E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.232**	**1.9E-3**	**3.2E-4**	**1.9E-3**	**1.2E-3**

TABLE B-W4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W4	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.092	7.8E-4	1.2E-4	0	4.9E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.124**	**9.4E-4**	**1.7E-4**	**1.9E-3**	**6.4E-4**

TABLE B-W5. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W5. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W5. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W5	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	HR000	Haul Roads	0.101	8.6E-4	1.3E-4	0	5.4E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.133**	**1.0E-3**	**1.9E-4**	**1.9E-3**	**6.9E-4**

TABLE B-B1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-B1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-B1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: B1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	9.2E-3	4.4E-5	6.9E-6	0	2.8E-5
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	STKP	PC Stockpile	5.7E-3	2.7E-5	4.3E-6	0	1.7E-5
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.117	9.9E-4	1.5E-4	0	6.2E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.149**	**1.1E-3**	**2.1E-4**	**1.9E-3**	**7.7E-4**

TABLE B-B2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-B2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-B2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: B2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	9.2E-3	4.4E-5	6.9E-6	0	2.8E-5
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.030	2.5E-4	4.0E-5	0	1.6E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.061**	**4.1E-4**	**9.2E-5**	**1.9E-3**	**3.1E-4**

Appendix C – TAP Modeling Results

TABLE C. TAP Maximum Modeled Concentrations and AACs

	TAP Maximum Modeled Concentrations by Model Scenario																	
	Y1	Y2	Y3	H1	H2	H3	H4	W1 [2]	W2 [2]	W3 [2]	W4 [2]	W5 [3]	B1	B2	Max Scenario			Compl-
Pollutant	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	ID	AAC [4]	iance
Aluminum	1.13561	1.41646	1.13855	1.19028	1.28403	1.09010	1.17371	6.01079	5.27252	6.00999	4.97175	6.17075	1.17437	0.97352	6.17075	W5	500	Yes
Arsenic [1]	0.00030	0.00049	0.00029	0.00023	0.00053	0.00020	0.00021	0.00091	0.00095	0.00090	0.00087	N/A	0.00024	0.00012	0.00095	W2	0.0023	Yes
Barium	0.01279	0.01595	0.01282	0.01341	0.01446	0.01228	0.01322	0.06773	0.05941	0.06772	0.05602	0.06953	0.01323	0.01097	0.06953	W5	25	Yes
Beryllium [1]	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00001	0.00001	0.00001	0.00001	N/A	0.00000	0.00000	0.00001	W1	0.042	Yes
Cadmium [1]	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000002	0.000002	0.000002	0.000002	N/A	0.000000	0.000000	0.000002	W1	0.0056	Yes
Calcium Carbonate	0.34375	0.33431	0.37347	0.39124	0.38168	0.37132	0.38141	1.18652	1.04095	1.18637	0.98165	1.21807	0.39107	0.34851	1.21807	W5	500	Yes
Calcium Oxide	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	ALL	100	Yes
Cyanide	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	ALL	250	Yes
Formaldehyde [1]	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	N/A	0.00007	0.00007	0.00007	ALL	0.77	Yes
Iron	0.29143	0.36343	0.29219	0.30525	0.32952	0.27957	0.30100	1.54079	1.35154	1.54058	1.27445	1.58179	0.30110	0.24962	1.58179	W5	50	Yes
Manganese	0.00477	0.00595	0.00478	0.00500	0.00538	0.00458	0.00493	0.02531	0.02220	0.02531	0.02094	0.02599	0.00494	0.00410	0.02599	W5	250	Yes
Nickel [1]	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00001	0.00001	0.00001	0.00001	N/A	0.00000	0.00000	0.00001	W1	0.42	Yes
Phosphorus	0.01036	0.01293	0.01039	0.01088	0.01169	0.00996	0.01073	0.05502	0.04827	0.05502	0.04551	0.05649	0.01074	0.00891	0.05649	W5	5	Yes
Sulfuric Acid	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	ALL	50	Yes
Thallium	0.00016	0.00020	0.00016	0.00017	0.00018	0.00016	0.00017	0.00085	0.00074	0.00085	0.00070	0.00087	0.00017	0.00014	0.00087	W5	5	Yes
Vanadium	0.00045	0.00056	0.00045	0.00047	0.00051	0.00043	0.00046	0.00237	0.00208	0.00237	0.00196	0.00243	0.00046	0.00039	0.00243	W5	2.5	Yes

[1] Carcinogenic TAP concentrations adjusted for 70-year exposure, as discussed in Section 3.4.4.
[2] Carcinogenic TAP concentrations adjusted for the West End pit LOM production limit, as discussed in Section 3.4.5.
[3] Modeling Scenario W5 is eliminated for carcinogenic TAP compliance, as discussed in Section 3.4.5.
[4] The AACs for carcinogenic pollutants are increased by a factor of ten per IDAPA 58.01.01.210.12(b); T-RACT adjustment.

Appendix D – Electronic Files

The electronic modeling files, emission inventory file, and Addendum references can be accessed via the following link:

https://drive.google.com/drive/folders/1o0-uNIu5DRds8hLShaD_0nPEBnlEJFCQ?usp=sharing

CERTIFICATE OF SERVICE

I hereby certify that on October 4, 2024, a true and correct copy of the foregoing EXPERT DECLARATION OF IAN H. VON LINDERN, P.E., Ph.D. was served on the following by electronic service:

Office of Administrative Hearings
P.O. Box 83720
Boise, ID 83720-0104
filings@oah.idaho.gov

Dylan V. Lawrence
Hearing Officer
Varin Thomas, LLC
P.O. Box 1676
Boise, ID 83701
dylan@varinthomas.com

Paula Wilson
Hearing Coordinator
Energy and Natural Resources Division
Office of the Attorney General
1410 N. Hilton
Boise, ID 83706
paula.wilson@deq.idaho.gov

Michael A. Short
Hannah M.C. Young
Deputy Attorney General
Department of Environmental Quality
1410 N. Hilton
Boise, ID 83706
michael.short@deq.idaho.gov
hannah.young@deq.idaho.gov

Ann Yribar
Deputy Attorney General
Energy and Natural Resources Division
Office of the Attorney General
P.O. Box 83720
Boise, ID 83720-0010
ann.yribar@ag.idaho.gov

Krista K. McINtyre
W. Christopher Pooser
Wade C. Foster
Stoel Rives LLP
101 S. Capitol Blvd., Suite 1900
Boise, ID 83702
krista.mcintyre@stoel.com
christopher.pooser@stoel.com
wade.foster@stoel.com

s/ Julia Thrower
Julia S. Thrower